NATIONAL RESEARCH COUNCIL OF CANADA

ASSOCIATE COMMITTEE ON SCIENTIFIC CRITERIA
FOR ENVIRONMENTAL QUALITY

AMINOCARB: THE EFFECTS OF ITS USE ON THE FOREST AND THE HUMAN ENVIRONMENT

Subcommittee on Pesticides and
Industrial Organic Chemicals

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TERMS OF REFERENCE OF THE SUBCOMMITTEE ON PESTICIDES AND INDUSTRIAL ORGANIC CHEMICALS

(1) The preparation of reports critically evaluating and collating the available cause-effect relationships which permit the estimation of the environmental risks associated with the use of synthetic organic chemicals in Canada - these documents will provide criteria for the evaluation of both present and future use patterns, and

(2) the identification of gaps in available criteria and preparation of recommendations for future research in these areas.

To meet this mandate, the Subcommittee has identified a number of priority compounds for consideration. Comprehensive reports are prepared to bring into perspective the diverse and somewhat obscure observations found in the literature. The documents consist of reviews, summarizing the available criteria and the research required. They also contain as supporting material the available data on which the overview is based.

The mandate of the Subcommittee does not include the setting of objectives and standards, the development of risk assessment, or the establishment of registered uses for pesticides in Canada. Therefore, it does not permit consideration of the engineering, economic, or legal aspects. The Subcommittee is only concerned with scientific information and environmental criteria. The documents do provide one of the components necessary in the consideration and development of risk assessments. Other agencies, both federal and provincial, have the actual responsibility for making decisions about the uses of specific synthetic organic chemicals in Canada and hence they have the task of bringing about an acceptable balance between the risks and benefits associated with the use of such chemicals by our society.

Inquiries concerning the activities of the Subcommittee should be directed to the Environmental Secretariat of the National Research Council of Canada, Ottawa, Canada.

NOTICE ON SUBCOMMITTEE MONOGRAPHS CONTAINING INDUSTRIAL BIOTEST MATERIAL

Picloram: The Effects of Its Use as a Herbicide on Environmental Quality. 1974. NRCC No. 13684

Endosulfan: Its Effects on Environmental Quality. 1975. NRCC No. 14098

Fenitrothion: The Effects of Its Use on Environmental Quality and Its Chemistry. 1975. NRCC No. 14104

Fenitrothion: The Long Term Effects of Its Use in Forest Ecosystems - Current Status. 1977. NRCC No. 15389

Proceedings of a Symposium on Fenitrothion: The Long-Term Effects of Its Use in Forest Ecosystems. 1977. NRCC No. 16073

Bacillus thuringiensis: Its Effects on Environmental Quality. 1976. NRCC No. 15385

Polychlorinated Biphenyls: Biological Criteria for an Assessment of Their Effects on Environmental Quality. 1978. NRCC No. 16077

Ecotoxicology of Chlorpyrifos. 1978. NRCC No. 16079

Carbofuran: Criteria for Interpreting the Effects of Its Use on Environmental Quality. 1979. NRCC No. 16740

Approximately four years ago, it was recognized by Canadian and U.S. authorities that irregularities existed in some reports of animal studies carried out by Industrial Biotest Laboratories Incorporated of Northbrook, Illinois. A cooperative effort of Health and Welfare Canada and the U.S. Environmental Protection Agency to validate the studies indicates that safety evaluations of 97 pesticides are supported wholely or in part by studies from this contract laboratory. Audits of the individual studies indicate that a significant portion are invalid. These agencies have requested new studies when information central to the assessment of human safety is "suspect". Specific details of the concerns that form the basis of these requests are unavailable.

The following monographs of the NRC's Subcommittee for Pesticides and Industrial Organic Chemicals are affected: picloram, endosulfan, fenitrothion, Bacillus thuringiensis, polychlorinated biphenyls, chloropyrifos and carbofuran. These documents contain some toxicological studies conducted by IBT which must be considered as "suspect" in light of the present situation. Hence, until the matter of the validation has been clarified, particular caution should be maintained to avoid the use of criteria developed on the basis of the IBT material. As additional information on the situation and replacement studies become available, the Subcommittee intends to review the need for updates of individual monographs.

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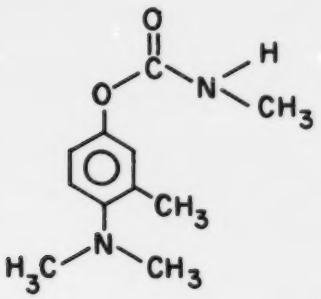
GLOSSARY

N.B. This glossary is not comprehensive. It includes terms used throughout the text. Expressions used rarely are defined where they appear in the text.

agl - above ground level
AI - active ingredient
BCF - bioconcentration factor
BW - body weight
CI - confidence interval
DClE - 1,2-dichloroethane
ED - electrochemical detector
EMC - encephalomyocardites
EPN - O-ethyl O-p-nitrophenyl phenyl phosphonothioate
EtAc - ethyl acetate
GC - gas chromatography
GLP - good laboratory practise
HPLC - high pressure liquid chromatography
K_{ow} - octanol:water partition coefficient
LC - lethal concentration
LD - lethal dose
NCV - nerve conduction velocity
NTE - neurotoxic esterase
RBC - red blood cell
RP - reverse phase
TLC - thin layer chromatography
TOCP - triorthocresyl phosphate
UV - ultraviolet
VSV - vesicular stomatitis virus

1.0 INTRODUCTION, OVERVIEW AND RECOMMENDATIONS

p-Dimethylamino-m-tolyl N-methylcarbamate



Aminocarb is a broad-spectrum insecticide used throughout the world for the control of agricultural and forest pests. It was originally developed by Farbenfabriken Bayer GmbH, Leverkusen, West Germany. In Canada, it is formulated and marketed by Chemagro Ltd. and is registered for the control of spruce budworm (Choristoneura fumiferana (Clem.)) in coniferous forest. It is not used as an agricultural insecticide in Canada. A temporary registration for forestry use was issued by Agriculture Canada in 1973 and full registration followed by 1977. Three products have Canadian registration - Matacil 1.8D oil-soluble concentrate (OSC) containing 1.8 lb aminocarb per gallon (216.6 $g.L^{-1}$) and the insecticide diluent 585; Matacil 1.8 OSC which does not contain diluent 585; and the older formulation, Matacil 1.68 OSC. The rates permitted in Canada are 52 to 87 g active ingredient (AI) in 1.1 to 1.4 L per hectare (ha). Repeat applications may be made provided there is a minimum 5-day interval between applications.

1.1 HISTORY OF USE IN CANADA

The first recorded Canadian use of formulated aminocarb was in Manitoba in 1965, where it was applied against fall cankerworm Alsophila pometaria, at 1134 $g\text{-}AI.ha^{-1}$ (Nigam 1975). In 1967, it was used against the jack-pine budworm, Choristoneura pinus pinus Freeman, in Manitoba (DeBoo and Hildahl 1967). Formulated aminocarb was first field tested against spruce budworm in 1970 in New Brunswick and was first used on an operational scale in 1975. Since then, its use has increased steadily, to the point where it is now one of the two insecticides routinely used to protect spruce-fir forests from feeding damage by spruce budworm. The other major forest insecticide used in Canada is the organophosphorus insecticide, fenitrothion.

Aminocarb's most extensive use has been in Quebec, New Brunswick and Newfoundland, where it has been employed either alone, or in combination with fenitrothion or phosphamidon. In Ontario, aminocarb has been the major chemical insecticide used against spruce budworm since 1976. In the decade since its first large-scale use, a total of about one million kg of aminocarb (active) has been applied in four eastern provinces - Newfoundland, New Brunswick, Quebec and Ontario (Nigam 1980). Appendix I provides a summary of aminocarb use in eastern North America since 1970.

Large-scale spraying programs against the spruce budworm have only one objective, viz protection of the current year's foliage. Control or suppression of the budworm outbreak is not the prime objective. Thus aminocarb, like most insecticides used today, is applied with the purpose of minimizing damage to the new growth produced each year (e.g. Prebble 1975). Timing of application is therefore important. For many years, the province of Quebec sprayed budworm larvae just as they emerged from their overwintering hibernacula, i.e. early May. More recently however, Quebec has adopted timing similar to other jurisdictions (Desaulniers 1977). Depending on local weather conditions, spraying programs usually start in the latter half of May and terminate about the third week of June. Spraying in Ontario and Newfoundland is often somewhat later than in Quebec and New Brunswick, starting in early June and finishing in late June or early July. Because the objective is to protect discrete forest areas, it is common for some areas to be treated once or twice in most years, depending on the hazard posed by budworm from year to year, and on the condition of the trees.

1.2 MANDATE

The NRC mandate to the Panel was to prepare a comprehensive critical review of the scientific literature on aminocarb and to present an overview of the factors needed for developing criteria that will enable the impact of aminocarb in the Canadian environment to be assessed.

1.3 CRITIQUE AND RECOMMENDATIONS

Aminocarb kills budworm by virtue of being a cholinesterase inhibitor. It is a wide-spectrum biocide and, like other chemicals used in the budworm control program, it is toxic at some dose to all organisms tested. The degree of exposure and the sensitivity of the organism are critical in any assessment. For example, certain non-target organisms (e.g. some other insects) are as sensitive as the budworm but mammals are less sensitive. It is this differential in sensitivity and exposure which underlies the philosophy of using such a compound for insect control.

The toxicity of a pesticide is often a function not only of the nature of the active ingredient but also of the formulation and its age and storage history. This is so with the current aminocarb formulation, for the solvent nonyl phenol is considerably more toxic to certain aquatic species than is the active ingredient. Obviously the usefulness of studies on any biocide can be seriously undermined if the formulation used is not thoroughly defined. In the case of aminocarb both the technical material and the formulated product have been used for toxicological studies with laboratory animals. Field studies on aminocarb have often been reported without mention of the formulation, thereby making them difficult to interpret reliably.

1.3.1 DISTRIBUTION AND PERSISTENCE

Like all chemicals used for budworm control, aminocarb is aerially applied over vast areas of forest. This type of application is not amenable to fine control and site-specific deposit can vary widely, perhaps by as much as 100%. The deposition pattern is affected by numerous factors, including the nature of the formulation, the application technology, topography and weather. It is impossible to develop a basis for predictions unless these variables are kept as similar as possible and are well defined in each study.

After a chemical is deposited, its sequestering pattern in the environment is characterized as much by the properties of the environment as by the properties of the chemical. It is generally possible to generate an adequate data base on a chemical's properties, although such data bases are not usually available at this time. It has been suggested (Klein et al. 1981) that a data base that includes the octanol-water partition coefficient, vapor pressure, absorbance spectrum, rate constants for hydrolysis as a function of pH, etc. is a general requirement for a preliminary characterization of a chemical's fate. This data base is required for all components of a formulation, not just the active ingredient. Accurate descriptions of the environment are much harder to generate. When a chemical is applied over a vast area, it encounters an infinitely varied range of environmental conditions, so that it may be theoretically impossible to make highly resolved holistic fate predictions with any degree of confidence. However, in cases where adequate chemical data bases do exist, it is possible to make preliminary predictions by considering only the gross characteristics of a specific ecosystem. For example, the octanol-water partition coefficient (K_{ow}) of an organic chemical can be used to estimate its general sequestering pattern in aqueous and nonaqueous compartments, albeit the effect of ion concentration and adjuvants on K_{ow} is not usually known.

Once the sequestering pattern of a chemical has been determined for a specific ecosystem, the relative importance of the operative degradative and removal processes can be considered and the

overall persistence in the system estimated. It is important that the limitations imposed by the sheer complexity of the task of assessing pesticide use in forest ecosystems be recognized by the assessor. Even if general patterns can be identified, subtle questions will remain. A social-political decision must be made as to what degree of resolution is acceptable for risk-assessment purposes.

The current data base indicates that the major transformation processes for aminocarb are hydrolysis and oxidation. The half-life ($t_{½}$) for oxidation in vitro is reported to be ~ 2 h. Hydrolysis is pH dependent, proceeding more rapidly in alkaline than in acidic solutions ($t_{½}$ at 20°C and pH 9 is < 6 d; $t_{½}$ at 20°C and pH 5 is approximately 90 d). However, little is known about the potential role of photolysis or microbial processes. To date, studies on photodegradation have not been carried out under environmentally relevant conditions, i.e. laboratory studies have generally involved illumination with artificial light of a different spectrum from that of sunlight. Also, the role of sensitizers in the natural environment has not been investigated. Although microbial degradation has not been directly investigated, it is conceivably a significant removal process as aminocarb is generally readily metabolized. The vapor pressure of aminocarb is low (1.7×10^{-5} mm Hg[α] at 20°C) so that volatilization will generally proceed quite slowly.

Hydrolysis will obviously be more important in an alkaline than in an acidic water body. Since boreal forest waters and soils tend to be slightly acidic, the relative importance of hydrolysis will be diminished. The rate at which photodegradative reactions proceed depends on the quantity and intensity of light reaching the chemical. It has been speculated that photodegradation could be responsible for some transformation of aminocarb in the atmosphere soon after its release from the aircraft. Even volatilization could become relatively important in certain situations, e.g. if a mass of aminocarb was spread over a large surface area such as an oil slick on a pond. If microbial degradation occurs, the rate will depend on whether the chemical is sequestered in an aerobic or anaerobic environment as well as on the microbial density.

Field and modelling studies predict that the $t_{½}$ is less than 11 d in most compartments. However, there are some data that suggest persistence of low levels from year to year in fir needles and associated compartments (e.g. ground vegetation, the organic layer of soil).

Very little is known about the persistence or sequestering patterns of the current adjuvants, diluent 585 and nonyl phenol.

[α] 1.7×10^{-5} mm Hg = 2.3×10^{-3} Pa.

The panel is concerned that many of the aminocarb transformation products have not yet been identified, much less evaluated for their toxicity.

The panel recommends the following studies to help clarify the persistence characteristics of aminocarb:

1. THE ROLE OF PHOTOLYSIS SHOULD BE QUANTIFIED IN TERMS OF THE LEVELS OF SENSITIZERS IN THE NATURAL ENVIRONMENT.

2. THE OCCURRENCE AND, WHERE APPROPRIATE, THE KINETICS OF MICROBIAL DEGRADATION SHOULD BE DETERMINED FOR REPRESENTATIVE ENVIRONMENTAL SITUATIONS.

3. THE PRODUCTS OF THE MAJOR DEGRADATIVE REACTIONS OPERATIVE IN THE ENVIRONMENT SHOULD BE IDENTIFIED (IF THEY OCCUR IN SIGNIFICANT QUANTITIES) AND THEIR TOXICITIES SHOULD BE DETERMINED. METHODOLOGY SHOULD BE DEVELOPED AS APPROPRIATE.

4. THE PERSISTENCE OF AMINOCARB AND ANY TOXIC BREAKDOWN PRODUCTS SHOULD BE FURTHER INVESTIGATED IN COMPARTMENTS WHERE THEY ARE LIKELY TO PERSIST. THESE COMPARTMENTS INCLUDE CONIFEROUS TREE FOLIAGE AND THE ORGANIC SOIL LAYER (INCLUDING LEAF LITTER).

1.3.2 ENVIRONMENTAL IMPACT

The actual impact of a pesticide, such as aminocarb, in a forest ecosystem depends on the interactions between it and the vulnerable receptors which are exposed. These interactions are determined not only by the distribution and fate of aminocarb in the environment but also by the timing of the exposure relative to an organism's life cycle, the relative sensitivity of the various organisms exposed, the interactions of the affected organisms with other members of the community, etc. The latter variables in ecosystem interactions are even harder to define than those related to persistence and fate.

While some primary effects of pesticides can be identified and discussed at the organism level, secondary and long-term effects can be discussed only in terms of the gross ecology of the area. This makes most effects impossible to conceive, much less detect, in areas where the baseline ecology, natural population fluctuations, etc. have not been characterized. Unfortunately, it is generally accepted that current techniques allow such characterization only for specific subsets of the ecosystem.

It is the opinion of the panel that monitoring studies are likely to elucidate an impact only if they concentrate on appropriate

indicators. If an organism or process is known to be relatively sensitive to aminocarb, is likely to be exposed to a relatively high concentration, or frequents a compartment in which aminocarb is relatively persistent, it is a likely indicator.

In the case of aminocarb, organisms are likely to encounter relatively high concentrations in the forest canopy or in open areas not protected by the canopy (Section 4.1) while more persistent residues may be encountered in the compartments associated with coniferous foliage and litter. The relative sensitivity of receptor organisms to aminocarb may be determined by either the chronic or the acute toxic response depending on the nature and length of the exposure and the exposure route. It is tempting to make certain generalizations, e.g. that smaller animals, with higher surface-to-volume ratios and relatively higher metabolic rates, are more sensitive, but supporting toxicological data are not available. Such generalizations, if validated, could greatly reduce the complexity of the problem.

The impact of aminocarb has been at least partially elucidated. It is known to have at least a short-term impact on other insects, especially certain budworm predators. For example, the populations of some spider species may be greatly reduced in sprayed plots. Whether or not there is a long-term impact on species' diversity remains to be established. There are some data to indicate that the percent parasitism of budworm pupae is reduced by aminocarb spraying, but monitoring studies have been limited to "before versus after spray" counts, generally incidental to efficacy studies. This issue could best be answered by between-generation comparisons of parasitism. Aminocarb applied at current operational doses also adversely affects honeybees and solitary bees directly exposed to spraying. No significant impact has been detected on bumblebees.

Adverse effects on birds have not been detected in the field (e.g. only one possibly intoxicated bird has been found in an aminocarb treated plot), but it must be borne in mind that predators would quickly remove dead or sick birds so that, using current census techniques, a lethal impact is likely to be detected only if it is catastrophic. Bird song is also a gross measure and the timing of the spray program is such that reductions could be masked by returning migrants, or other factors. Other direct signs of carbamate toxicity, such as cholinesterase inhibition or behavioral effects, are reversible and hence are difficult to monitor; the absence of such effects is not a definite indicator of no-effect. For these reasons the panel suspects that anything other than a major impact might not be detected using current monitoring techniques. The fact that these techniques have demonstrated an effect in the case of fenitrothion (NRCC 1975) allows some perspective for comparison. Toxicology and exposure studies, considered together, indicate that birds which frequent the crown canopy or feed on contaminated prey may, in the worst-case, be exposed to doses of aminocarb near the LD_{50}. The panel therefore considers that there may in fact be some nondetected impact on avian species, with crown-canopy

birds and nestlings probably being the most vulnerable and hence potential indicators deserving additional attention.

Organisms which inhabit the compartments where aminocarb is suspected to persist have not been adequately monitored to permit reliable assessments. Organisms deserving more attention include those responsible for decomposition processes in leaf litter and other organisms inhabiting the organic soil layer (e.g. ants, mites and fungi). In one study aminocarb reportedly had little effect on pond microbial communities while, in another study, oxygen consumption increased; these data cannot be extrapolated to allow generalities about aminocarb.

Notwithstanding the importance of establishing a rational, sequential approach to monitoring, aminocarb is currently in large-scale use and suspected effects deserve immediate close scrutiny. The panel recommends that:

5. MONITORING OF THE FOLLOWING ORGANISMS AND PROCESSES SHOULD BE GIVEN, OR CONTINUE TO BE GIVEN, HIGH PRIORITY:

   - ORGANISMS AND DECOMPOSITION PROCESSES IN THE ORGANIC SOIL LAYER AND LEAF LITTER IN CONIFEROUS FORESTS
   - CROWN-CANOPY BIRDS AND NESTLINGS
   - POLLINATORS, POLLINATION AND THE RELATED PROCESS OF FRUIT-SET
   - BUDWORM PREDATORS AND SPIDERS. STUDIES SHOULD MONITOR SPECIES DIVERSITY IN THE MEDIUM AND LONG-TERM.
   - BUDWORM PARASITES

It is the opinion of the panel that careful monitoring, focused on likely indicators, can elucidate any immediate, gross impact. However, the panel has little confidence that subtle or long-term impact can neccesarily be detected with current techniques, especially if an area is not treated or monitored consistently from year to year. The panel is very aware of the generally applicable maxim that lack of detection of an effect does not necessarily mean that the effect does not exist!

The panel thus considers certain issues to be impossible to address with any degree of certainty at the present time. These issues include the following questions:

- does aminocarb cause any short- or long-term sublethal effects such as reduction in species diversity or deleterious changes in predator-prey balances?

- could such effects be magnified by repeated annual application of aminocarb?

- could such effects be magnified by interactions with other pesticides and pollutants?

These issues can be resolved only in terms of the impact on the total forest ecosystem. The panel believes that the situation is too complex, and the area affected too diverse and too vast, to realistically expect that high-resolution answers can be obtained. Again, resource managers and regulatory agencies must make some decision as to what degree of resolution and hence margin of safety is acceptable.

The panel believes the situation will improve only if management strategies are developed which minimize the need for large-scale spray operations with aminocarb or with any other nonspecific biocide. In other words, only when the size of the spray programs, and hence the need to consider the long-term consequences of such programs at the ecosystem level, are minimized will assessments significantly improve. Potential strategies have been discussed by Baskerville (1976).

IT MUST BE EMPHASIZED THAT THE ABOVE POINTS DO NOT SPECIFICALLY APPLY TO AMINOCARB. IN FACT, AT THE DEGREE OF RESOLUTION PRESENTLY ACHIEVABLE, THE DETECTED SHORT-TERM IMPACT OF AMINOCARB IS BETTER DOCUMENTED AND APPARENTLY LESS SEVERE THAN THE IMPACT OF CERTAIN ALTERNATIVE CHEMICALS AT OPERATIONAL DOSAGES (e.g. FENITROTHION, NRCC 1975).

1.3.3 AQUATIC IMPACT

The direct application of aminocarb to large water bodies is generally avoided in Canada. However, it is the experience of the panel that spray is often not shut off over small ponds and streams. All water bodies may be contaminated through spray drift and runoff and, as well, contamination often results from human error or overspray.

Monitoring studies suggest that concentrations of aminocarb in natural woodland waters rarely exceed 10 $\mu g.L^{-1}$, although considerably higher concentrations have been occasionally cited. However, most of these monitoring studies were overviews and the panel is concerned that higher concentrations could occur in water bodies not protected by the forest canopy or due to local partitioning of oil-based formulations. It is recommended that:

6. THE POSSIBLE OCCURRENCE OF LOCALIZED HIGH CONCENTRATIONS OF AMINOCARB BE INVESTIGATED, PARTICULARLY IN UNPROTECTED STANDING WATER.

Nonyl phenol, one of the current adjuvants, is of particular concern with regard to aquatic ecosystems. In flowing water, nonyl

phenol residues are reported to be transient and concentrations are generally less than 10 $\mu g.L^{-1}$. However, in standing water an extremely high concentration (1100 $\mu g.L^{-1}$) was measured soon after spraying. The panel is concerned that the data base on nonyl phenol is too limited to draw any firm conclusions on distribution and persistence. It is recommended that:

7. AS LONG AS NONYL PHENOL REMAINS IN USE, MONITORING STUDIES SHOULD MEASURE RESIDUES OF NONYL PHENOL AS WELL AS OF THE ACTIVE INGREDIENT.

The relative toxicity of the various components of aminocarb formulations to a wide range of aquatic organisms has been established in laboratory tests.

Some aquatic organisms are more sensitive to nonyl phenol than to aminocarb, so that formulations containing nonyl phenol can actually be more toxic than the pure active ingredient. The LC_{50} of the 1.8D formulation is reported to be as low as 300 $\mu g.L^{-1}$ for rainbow trout, 20 $\mu g.L^{-1}$ for crustacea and 100 $\mu g.L^{-1}$ for algae. The 1.8F formulation, which does not contain nonyl phenol and is not in operational use, is reported to be considerably less toxic to some aquatic organisms than is the 1.8D formulation. These data are preliminary.

Residue data indicate that spraying with the 1.8D formulation at 70 $g.ha^{-1}$ may result in concentrations in natural waters that are toxic to some organisms. The panel was particularly concerned that phytotoxic concentrations of nonyl phenol have been measured in shallow standing water following spraying. The toxicity to crustacea is also of concern when related to field concentrations expected from operational spraying at 70 $g.ha^{-1}$.

Field studies have elucidated few effects, possibly because they are so difficult to interpret. For example, the methods used are often inadequate or the formulation used or dose encountered are not clearly specified. So far, fish kills have not been associated with aminocarb spraying in Canada, but sublethal fish responses have been observed using analysis of stomach contents and cholinesterase activity. Field studies suggested a threshold of 30 $\mu g\text{-}AI.L^{-1}$ for effects on drift of benthos and a threshold of about 100 $\mu g\text{-}AI.L^{-1}$ for an increase in O_2 consumption by microorganisms.

1.3.4 MAMMALIAN TOXICOLOGY

The mammalian toxicology data base for aminocarb is "state-of-the-art" and the panel is generally satisfied with the quality of the studies.

The acute toxicity of aminocarb to laboratory mammals is quite well defined. The acute oral LD_{50} has been reported to range from 19 to 60 mg-AI.kg-BW^{-1} for a variety of laboratory mammals. Generally, rats were less sensitive than mice or higher mammals. The acute dermal LD_{50} has been reported to range from 31 to 500 mg-AI.kg-BW^{-1} and the reported LD_{50} for intraperitoneal (ip) administration ranges from 5 to 21 mg-AI.kg-BW^{-1}. In most cases the slope of the dose-response curve has not been reported in the open literature, and thus the potential impact of localized variations in the amount deposited in the field cannot be easily addressed. The panel suggests that in future, the slope of the acute dose-response curve should be reported when an LD_{50} experiment is conducted.

No-observed-effect-levels (NOEL's) and observed-effect-levels for subacute and chronic dosing are summarized in Table 1-1. Aminocarb does not appear to be carcinogenic or mutagenic. The data in Table 1-1 suggest that, under conditions of repeated exposure, effects such as reduced weight gain and histopathological changes are associated with doses similar to those that induce only mild symptoms of cholinesterase inhibition. This suggests that the dose-reponse curve is steep.

Aminocarb has not been shown to cause any significant teratogenic effects in rats. However, the experiments do not meet current protocols and the panel believes updated studies would be useful. New studies are being conducted at this time.

Under current use-patterns of aminocarb, human bystanders are exposed to acute rather than chronic dosing. The computer-predicted total human bystander exposure is 7×10^{-3} mg-AI.kg-BW^{-1}, nearly all of which is received via the dermal route. There is no validation for this number and it is not known how much of this dermal dosage is absorbed. The deposited dosage is about 300-fold lower than the reported NOEL for subacute oral exposure of rats and about 4000-fold lower than the reported NOEL for dermal exposure of rats. However, the computer scenario assumes a uniform droplet concentration within the swath; calculations with the approximate distribution resulting from the vortex wakes of the spray planes indicated spatial variations in exposure of 100% of the above figure. Also, human error can lead to oversprays and spillage can result in very large localized deposits.

Clearly, certain human populations receive a greater than average exposure. These include workers in pesticide manufacturing plants, formulators and spray operators. It is recommended that:

8. CAREFUL DOCUMENTATIONS OF SPILLS BE IMPLEMENTED, PARTICULARLY WITH FOLLOW-UP STUDIES ON THE HEALTH OF THE PERSONNEL WHO CLEANUP THE SPILL.

9. WORKER EXPOSURE SHOULD BE MEASURED ROUTINELY AND CORRELATED TO ANY RELATED HEALTH EFFECTS.

Table 1-1. Summary of the no-observed-effect levels (NOELs) and the observed-effect levels for subacute and chronic mammalian exposure to aminocarb.

Type of study	Species	Duration	Route	NOEL	Effect level	Observed Effect
				mg-AI.kg-BW^{-1}.d^{-1}		
Subacute toxicity	Rat	4 mo	oral	10	20	Inhibition of serum cholinesterase Reduced weight gain
	Dog	3 mo	oral	<5	5-10	Clinical signs of cholinesterase inhibition
	Cat	10 d	oral	5	10	Clinical signs of cholinesterase inhibition 1 of the 2 cats died after 3 days
	Rat	2 mo	intraperitoneal	2	4	Reduced weight gain
	Rat	21 d	dermal	30	60	Clinical signs of mild cholinesterase inhibition
Chronic toxicity	Rat	84 weeks	oral	5	10-20	Histopathological changes Reduced weight gain
	Dog	2 years	oral	2-4	10	Slight clinical signs of cholinesterase inhibition Reduced weight gain
Reproduction	Rat	3 generations	oral	10	40 (maternally toxic dose)	Reduced litter size and weight (statistically significant for the F_{3b} litter only) Reduced pup weights at weaning[α]

[α] Although not statistically significant, a similar tendency was noted in F_{1a}, F_{1b} and F_{2a} offspring at 10 mg-AI.kg-BW^{-1}.d^{-1}.

The panel is aware that these workers are often exposed to many chemicals, making it difficult to draw conclusions on related health effects.

The dermal LD_{50} varies considerably for different formulations tested. The toxicity may be due to any or all of the components in the formulations used in these studies. The efficiency of the percutaneous absorption of aminocarb is not known. The efficiency of absorption of the active ingredient might be influenced by other components of the formulation. It is recommended that:

10. THE EFFICIENCY OF PERCUTANEOUS ABSORPTION SHOULD BE MEASURED FOR TECHNICAL AMINOCARB AND FOR AMINOCARB IN COMBINATION WITH FORMULANTS.

Nonyl phenol is a mild-to-moderate skin irritant. The panel recommends that:

11. EXPOSED WORKERS BE SPECIFICALLY MONITORED FOR SKIN IRRITATION, PARTICULARLY WHEN NONYL PHENOL IS USED.

It is generally assumed that tissue cholinesterase inhibition is the mechanism of toxicity of aminocarb and other anticholinesterase pesticides. The panel thus found it curious that there was no potentiation, in terms of increased deaths, when rats were given half the LD_{50} dose of aminocarb simultaneously with each of 15 other anticholinesterase pesticides. While this is not a high priority item, the panel recommends that:

12. MORE PRECISE TESTING BE CONDUCTED TO BETTER ELUCIDATE THE INTERACTION BETWEEN CARBAMATE PESTICIDES SUCH AS AMINOCARB AND OTHER ACETYLCHOLINTERASE INHIBITORS.

The panel considered the recurring question of whether the spray program could in any way be implicated in the causation of the children's disease, Reye's syndrome. The panel found no evidence to suggest any connection between Reye's syndrome and aminocarb spraying. The panel suggests that a national survey of the incidence of Reye's syndrome could provide a definitive answer to the question of whether there is a potential association of the disease with the spray program; at the same time such a survey would increase the medical community's awareness of the disease and perhaps eventually lead to a higher incidence of earlier diagnoses with the resulting improved prognosis.

The panel also suggests that research attention would be more productively focused on the broader question of whether there is synergism between emulsifiers in general and other toxicants. This is important because of the wide use of emulsifiers in household products.

1.3.5 ANALYSIS

The relatively few analytical methodologies available for aminocarb and its metabolites generally reflect the "state-of-the-art" for carbamates. However, there is sufficient variation in analytical techniques to raise concern regarding the comparability of data from different laboratories. In general, there are four major sources of variability in aminocarb residue analysis; sampling, method, analysis and misinterpretation of analytical data. At $mg.kg^{-1}$ levels, sampling is likely to be the major source of variation (Section 5.4.4). Storage of samples is also a potential source of variation as aminocarb can be appreciably degraded in chlorinated organic solvents or acetone. It is recommended that:

13. a) GOOD LABORATORY PRACTICE ALWAYS BE IMPLEMENTED (AS DETAILED IN SECTION 2.4.4). INTERLABORATORY STUDIES SHOULD BE CARRIED OUT BETWEEN LABORITORIES ENGAGED IN AMINOCARB RESIDUE ANALYSIS, WITH PARTICULAR FOCUS ON THE VERIFICATION OF SAMPLING TECHNIQUE.
    b) STORAGE SOLVENTS BE CHOSEN CAUTIOUSLY.

14. THE ANALYSIS OF POTENTIALLY TOXIC METABOLITES SHOULD BE INCLUDED IN ANY RESIDUE METHOD.

15. RESIDUE METHODOLOGY FOR ASSAYING WORKER EXPOSURE BE DEVELOPED AND IMPLEMENTED.

2.0 CHEMISTRY

2.1 CHEMICAL, PHYSICAL AND SPECTRAL PROPERTIES OF ACTIVE INGREDIENT

2.1.1 SOLUBILITY

The chemical and physical properties of aminocarb are summarized in Appendix II.1. Aminocarb is readily soluble in polar organic solvents, moderately soluble in aromatic solvents and slightly soluble in water (2000 $mg.L^{-1}$; Mobay 1979).

The partition coefficient between octanol and water (K_{ow}) has been determined using gas chromatographic (GC) analysis of the concentrations in each phase. The K_{ow} is pH dependent (Appendix II). At pH 8, when aminocarb is in the free base form, K_{ow} = 70 ± 10 (Weinberger and Greenhalgh 1981). McLeese et al. (1979) have predicted that log K_{ow} = 2.91 (K_{ow} = 813), based on Hansch substitutent values. Mackay et al. (1980) attempted to relate the octanol-water partition coefficient to aqueous solubility as follows:

$$\ln K_{ow} = 7.494 - \ln C^S + 6.79\ (1 - T_m/T)$$

where C^S is the aqueous solubility for solids in $mol.m^{-3}$, T is the temperature (°K) and T_m is the melting point (°K). At 25°C, assuming that the solubility is 2000 $mg.L^{-1}$, log K_{ow} would be 1.6. This value is in good agreement with the experimental value of Weinberger and Greenhalgh (Appendix II).

2.1.2 ADSORPTION

(i) Soil - In the concentration range 0.25-5.0 $mg.kg^{-1}$, at 25°C, about 75% of aminocarb was bound to a loam soil (4.2% organic matter) (Atwell 1978); the Freundlich constants, K and 1/n, were 12.9 and 0.9 respectively. In this study the soil-water mixtures (10 g:50 g) were shaken for 16 h; the kinetics of adsorption were not determined.

(ii) Polymers - Weinberger and Ouellette (1981) have shown that aminocarb is extensively adsorbed (47%) from water onto Tygon® after 24 h, but adsorbed to lesser extents (6%, 0.01%, 0.01%) to Teflon®, Parafilm® and polyethylene respectively.

2.1.3 VOLATILIZATION

2.1.3.1 Solid Surfaces

Abdel-Wahab et al. (1966) found that the volatilization of aminocarb from a glass surface at 25°C was a first-order process (70-80%

disappearance) with a half-life of 1.6 h. After about four hours there was evidence of formation of less volatile compounds, resulting from air oxidation or fluorescent light photolysis. The half-life for volatilization from leaves of bean plants was 4 h. This study was not done in the dark to separate the effects of air and light, nor were the less volatile products identified. There are no other data on volatilization from foliage, soil or water.

2.1.3.2 Water

In general, the rate of volatilization of a chemical from water depends, at least, on the depth of the water, the liquid-film and gas-film mass transfer coefficients, the vapor pressure and the aqueous solubility of the chemical (Mackay and Leinonen 1975; Smith et al. 1980). The ratio of the two latter parameters is known as the Henry's law constant, H. Smith et al. (1980) have suggested that compounds which have $H < 10$ torr.L.mol^{-1}[α] may be considered "low-volatility" compounds with little tendency to volatilize from water.

For aminocarb, H is about 2×10^{-3} torr.L.mol^{-1}[α] (calculated using a vapor pressure of 2×10^{-5} mm Hg[α] (Addison 1981b) and a solubility of 2000 mg.L^{-1}), which suggests that aminocarb would have little tendency to volatilize from water. However, aminocarb sprayed on the surface of water may volatilize quickly from the surface microlayer; such a phenomenon has been observed for fenitrothion (Maguire and Hale 1980).

2.2 SYNTHESIS OF AMINOCARB AND TRANSFORMATION PRODUCTS

2.2.1 AMINOCARB

In subsequent chapters the names of aminocarb derivatives and metabolites have been abbreviated. A key is provided, along with chemical abstracts usage and registry numbers, inside the back cover.

Aminocarb (A) may be conveniently synthesized from the corresponding phenol (4-dimethylamino-3-methylphenol (C)) by reaction with methyl isocyanate (CH_3NCO) (Figure 2-1, Scheme 1). This reaction provides a general route to N-methylcarbamates and, in the above case, proceeds smoothly in anhydrous diethyl ether in the presence of a catalytic amount of weak base. The commercially available 3-methyl-4-nitrophenol may be similarly esterified (Figure 2-1, Scheme 2) and the resulting adduct may be reduced catalytically in methanol (H_2/Pd, carbon, atmospheric pressure) to yield the free amine (AA). In the

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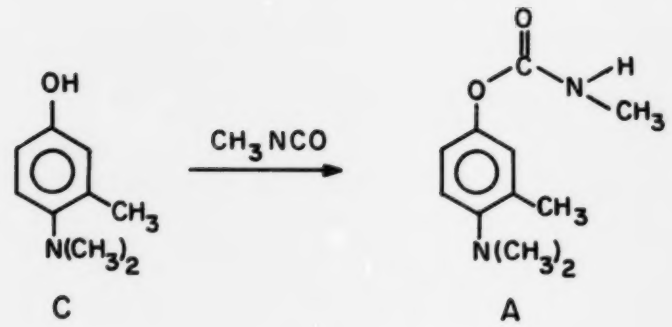
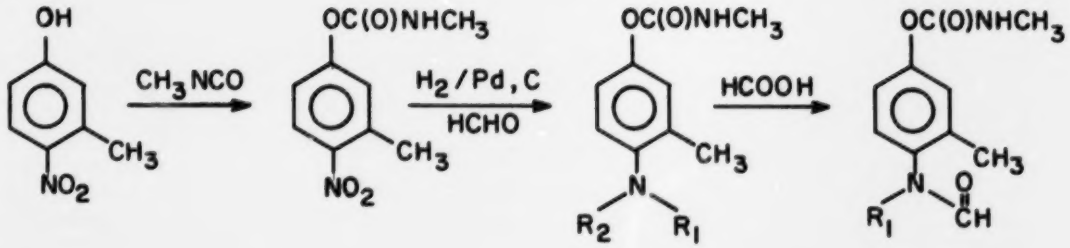
[α] 1 torr = 1 mm Hg = 0.133 kPa at 0°C.

Scheme 1



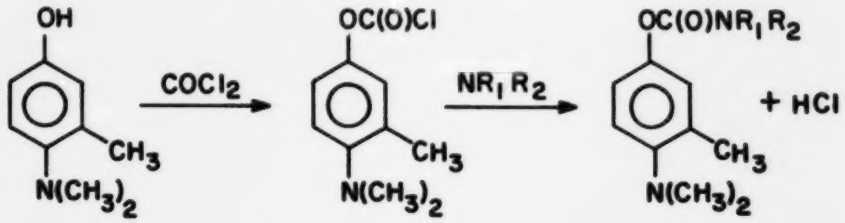
Scheme 2



A : $R_1 = R_2 = CH_3$
AA : $R_1 = R_2 = H$
MAA : $R_1 = H$; $R_2 = CH_3$

FA : $R_1 = H$
MFA : $R_1 = CH_3$

Scheme 3



Scheme 4

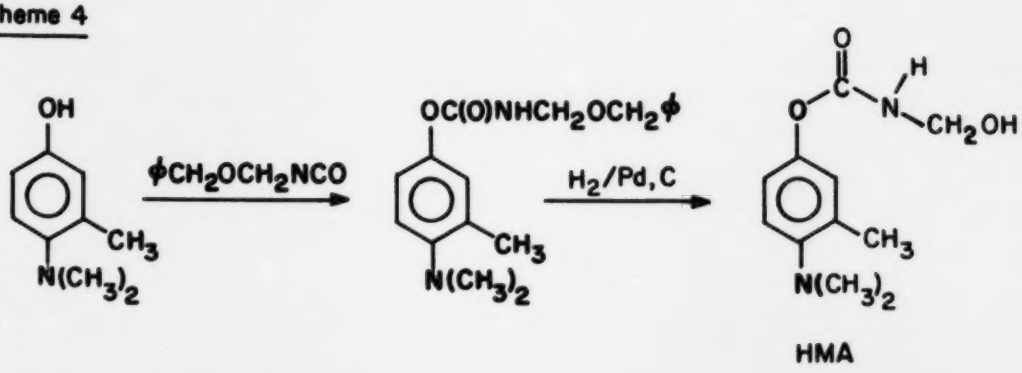


Figure 2-1. Synthesis of aminocarb and transformation products.

presence of an appropriate amount of formaldehyde, A or N-demethylated analog (MAA) may be readily obtained from this reaction. These products may serve as substrates for the further modification of the dimethylamino group of A. Products AA and MAA are readily N-formylated using formic acid, resulting in 4-formamido-3-methylphenyl-N-methylcarbamate (FA) and 4-methylformamido-3-methylphenyl-N-methylcarbamate (MFA).

Variation of the pattern of substitution on the carbamate nitrogen may be achieved in two stages. The phenol (C) (in an aromatic solvent) may be treated with phosgene in the cold to yield the corresponding acid chloride. This product may be derivatized in situ with an amine (after removal of the excess phosgene) to yield the corresponding carbamate (Figure 2-1, Scheme 3).

2.2.2 BY-PRODUCTS

The products AA, MAA, FA and MFA represent the major transformation products of A which retain an intact carbamate group and thus inhibit cholinesterase. A further transformation product, which has been identified in animal metabolism, is the carbamate N-hydroxymethyl analog (HMA) (Krishna and Casida 1966; Oonnithan and Casida 1966). This transformation product may be obtained by reacting phenol (C) with isocyanatomethylbenzyl ether to yield the corresponding ester (Figure 2-1, Scheme 4). Catalytic hydrogenation results in the desired product (HMA) (Balba and Casida 1968).

2.3 FORMULATION

Prior to 1977, a number of diluents (or carriers) were used in the operational aminocarb formulation for forest spraying. These included Dowanol TPM, Panasol, Summer Oil (a mixture of light boiling fractions) and Diesel Oil. In 1977 and 1978, No. 2 fuel oil was utilized but since then a more refined hydrocarbon fraction, diluent 585, has been used.

Nonyl phenol is added to all registered formulations as a primary solvent. The formulation in current use, the 1.8D oil soluble concentrate[α], consists of 19.5% (by weight) active ingredient, 30.0% diluent 585 and 50.5% nonyl phenol. In the field, additional diluent 585 is usually added to make a spray formulation containing 70 g aminocarb and 182 g nonyl phenol in 1 to 1.5 L. Some experimental formulations have contained different adjuvants. In 1981 a new aminocarb "flowable" formulation, which does not contain nonyl phenol, was introduced for experimentation. This formulation consists of finely milled aminocarb suspended in summer oil and is usually referred to as

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[α] The US 1.4D oil soluble concentrate is equivalent.

aminocarb 1.8F. In the field, additional diluent (585 oil, summer oil or water) is added.

2.3.1 DILUENT 585

Diluent 585 oil derives its name from the fact that it is the fraction of No. 2 fuel oil which distills at or below 585°F (308°C). It is composed of a mixture of alkylated benzenes and naphthalenes (Howse et al. 1978). Little is known about the identity, environmental reactions and persistence of the many components of 585 oil, including volatilization which may be an important route of dissipation. The specifications of diluent 585 are summarized in Appendix II.2.

2.3.2 NONYL PHENOL

Nonyl phenol is a mixture of monoalkyl phenols, predominately para substituted with about 3% of the ortho isomer and 4% 2,4-dinonylphenol. The side chains are random-branched alkyl groups. The specifications of a representative sample are listed in Appendix II.3.

2.4 ANALYSIS

2.4.1 TECHNICAL MATERIAL AND FORMULATIONS

2.4.1.1 Technical Grade

Five samples of Bayer technical aminocarb were analyzed by gas chromatography/nitrogen phosphorus detector (GC/NPD) for active ingredient (AI) using the trifluoroacetyl derivative and by direct measurement using high pressure liquid chromatography/ultraviolet detector (HPLC/UV) at 254 nm. The range of AI values was 96.2-97.6% with good agreement for both methods. The average 95% confidence levels were ±0.6% and 0.4%, respectively, for GC and HPLC methods (Patel 1978). HPLC would be the method of choice due to better precision and use of the underivatized material.

2.4.1.2 Formulations

Formulated aminocarb used in New Brunswick was analyzed by HPLC/UV and HPLC/electrochemical detector (ED) (Lanouette and Pike 1980). A buffered mobile phase, at pH 6.8 (MeOH:phosphate, 1:1), was necessary to obtain sharp peaks on a C_{18}-reverse phase column. Four random samples taken from the field in 1978 gave % AI values of 6.74 (1.5% coefficient of variation), 6.79 (2.1%), 6.85 (1.1%) and 6.89 (1.5%). The New Brunswick recommendations for aerial spray solutions suggest 6.8% AI. By the same procedure, six commercial formulations indicated to contain 19.5% AI by the manufacturer, gave an average value of 19.1 ± 2.3% with the UV detector and 19.32 ± 3.73% with the ED.

2.4.1.3 Impurities in Technical Aminocarb

Patel (1978) used both GC and HPLC methods to determine the impurities in the five Bayer manufactured samples of technical aminocarb. The mobile phase for HPLC was 2,2,4-trimethylpentane:dioxane, 9:1; flow rate 2 $mL.min^{-1}$ on a Porasil column. The retention times of compounds I, X, II, IX, VII (Table 2-1) were 2.2, 4.6, 5.4, 6.6, and 12.2 min, respectively. The other components were analyzed by GC. The structures and range of concentrations of the impurities found are given in Table 2-1. The toxicity of these impurities is not well defined.

2.4.2 RESIDUES

Unlike other carbamates, there are few analytical methods for aminocarb and its metabolites. The relevant ones are listed in Table 2-2. Sample matrices are predominantly those associated with the forest environment (i.e. soil, sediment, water, foliage) and aquatic plants and fish, together with crops and milk.

The methods are a reflection of the chromatographic "state-of-the-art" for carbamates. In general, these compounds are thermally unstable, as indicated by early methods involving detection of the hydrolyzed phenol (Olson 1964; Stanley and Delphia 1978) and later by derivatization of the carbamate moeity (Lawrence 1976; Sundaram et al. 1976). The availability of deactivated chromatographic supports and selective nitrogen detectors now permits the direct analysis of aminocarb and its metabolites by GC (Mamarbachi 1978; Sundaram et al. 1979). HPLC is also used for analysis (Brun and MacDonald 1978) but requires a greater concentration step in the method because of the lack of sensitive and selective HPLC detectors.

2.4.2.1 Extraction

Aminocarb is readily extracted from soil, foliage, aquatic plants and certain crops (corn, lettuce, carrots, turnips, cabbages, potatoes and wheat) by blending with polar organic solvents such as acetronitrile, methanol, acetone and ethyl acetate (EtAc). In soil, the presence of some water is helpful. Residues in sediment are more difficult to remove. Both methods quoted (Table 2-2) involve heating, either by soxhlet extraction or refluxing with NH_4Cl/EtAc. The method of Stanley and Delphia (1978) for fish involves refluxing with a mixture of 1,2-dichloroethane and methanol. However, better recoveries appear to be obtained by blending with ethyl acetate (Szeto and Sundaram 1980).

Use of a single-phase solvent system (methanol, methylene chloride and water) to remove the lipids from human and cow milk (Bligh

Table 2-1. Impurities in technical aminocarb (Patel 1978).

Compound	Substituent R_1	R_2	R_3	R_4	R_5	Concentration range (%)
I	$C(O)N(CH_3)$	CH_3	CH_3	$N(CH_3)_2$	H	0.08 - 0.16
II	$C(H)NHCH_3$	CH_3	CH_3	$N(CH_3)_2$	H	0.04 - 0.15
III	H	CH_3	H	CH_3	H	0.39 - 0.68
IV	H	CH_3	CH_3	$NHCH_3$	H	0.11 - 0.27
V	H	CH_3	H	H	H	0.00 - 0.27
VI	H	CH_3	H	$N(CH_3)_2$	H	0.40 - 0.50
VII	H	CH_3	CH_3	$N(CH_3)_2$	DMAC[α]	0.08 - 0.14
VIII	OH	CH_3	$NHCH_3$	H	H	0.00 - 0.12
IX	OH	CH_3	$N(CH_3)_2$	H	H	0.16 - 0.58
X	OH	CH_3	$N(CH_3)_2$	CH_3	H	0.09 - 0.27
XI	H	CH_3	$N(CH_3)_2$	H	H	0.30 - 0.47
XII	OH	CH_3	$N(CH_3)_2$	H	DMAC[α]	0.31 - 0.93
N,N[1]-dimethyl urea						0.11 - 0.24

[α] DMAC - p-dimethylamino-m-cresol.

Table 2-2. Analytical methods for aminocarb (abbreviations are defined in glossary).

Medium	Extraction	Clean-up	Derivative[α]	Technique	Recovery (%)	Detection Limit ($mg.kg^{-1}$)	Reference
Soil	Blend; CH_3CN/H_2O	Hydrolysis	4-amino-pyridine	Colormetric	90	0.1	Olson (1964)
	Blend; CH_3CN	Acid/base	HFB	GC/ECD	97	0.1	Sundaram et al. (1976)
	Blend; EtAc	Coagulation	-	GC/NPD	90	0.5	Szeto and Sundaram (1980)
	Reflux DCIE/CH_3OH	Acid/base, hydrolysis	2,4-DNB	GC/ECD	81	5.0×10^{-2}	Stanley and Delphia (1978)
	?	?	2,4-DNB	EC/GLC	?	1.0×10^{-2}	Stanley and Delphia (1981)
Sediment	SoxL/Acetone	Coagulation	-	GC/NPD	?	8.0×10^{-3}	Mamarbachi (1978)
	NH_4Cl/EtAc	CH_2Cl_2	-	HPLC/UV(RP)	?	0.5	Brun and MacDonald (1978)[β]
Water	Toluene	-	HFB	GC/ECD	101	1.0×10^{-4}	Sundaram et al. (1976)
	EtAc	-	-	GC/Hall[γ] and HPLC/UV	100	5.0×10^{-4}	Brun and MacDonald (1978)[β]
	CH_2Cl_2	-	-	GC/NPD		2.0×10^{-4}	Environmental Monitoring Committee (1979b)
	CH_2Cl_2	-	-	GC/NPD		1.0×10^{-5}	Mamarbachi (1978)
	XAD-2	-	-	GC/NPD/Hall[γ]	98	1.0×10^{-2}	Sundaram et al. (1979)[β]
	XAD-4	-	-	HPLC/Fluor(RP)	83	5.0×10^{-5}	Brun and MacDonald (1978)[β]
	EtAc	-	-	GC/NPD	101	2.0×10^{-5}	Weinberger et al. (1980)[β]
	CH_2Cl_2	Acid/base, hydrolysis	2,4-DNB	GC/EPD	97	1.0×10^{-2}	Stanley and Delphia (1978)
	?	?	2,4-DNB	EC/GLC	?	1.0×10^{-3}	Stanley and Delphia (1981)
Foliage	Blend; CH_3CN	Acid/base	HFB	GC/ECD	89	0.5	Sundaram et al. (1976)
	Blend; EtAc	Coagulation	-	GC/NPD	?	6.0×10^{-2}	Mamarbachi (1978)
	Blend; EtAc	Acid/base	-	GC/NPD	105	5.0×10^{-2}	Anon (1979)
	Blend; EtAc	Coagulation	-	GC/NPD	99	0.5	Szeto and Sundaram (1980)
	?	?	2,4-DNB	EC/GLC	?	$<1.0 \times 10^{-2}$	Stanley and Delphia (1981)
Human Milk	CH_3OH/ether	Acid/base	-	GC/NPD	84	2.0×10^{-3}	Newlands et al. (1979)
Aquatic Plants	Blend; EtAc	Acid/base	-	GC/NPD	?	5.0×10^{-2}	Weinberger et al. (1980)
Crops -corn -lettuce -carrots -turnips	Blend; Acetone	CH_2Cl_2/hexane	HFB	GC/Coulson[γ]	?	0.1	Lawrence (1976)
-cabbage -potato -corn -wheat	Blend; Acetone	CH_2Cl_2/hexane Florisil	-	HPLC/UV (RP)	>70	0.1	Lawrence (1977)
Fish	Reflux; DCIE/CH_3CN	Acid/base, hydrolysis	2,4-DNB	GC/ECD	78	5.0×10^{-2}	Stanley and Delphia (1978)
	Blend; EtAc	Coagulation	-	GC/NPD	98	0.5	Szeto and Sundaram (1980)
	?	?	2,4-DNB	EC/GLC	?	$<1.0 \times 10^{-2}$	Stanley and Delphia (1981)

[α] HFB = heptaflurobutaryl.
DNB = dinitrobenzene

[β] Includes metabolites.

[γ] Conductivity detector.

and Dyer 1959) was successful, but was discarded because of the large volumes of solvent required. Methanol:ether (15:11) followed by acid extraction proved to be adequate for the extraction of residues from human and cow milk. Interfering coextractants reduced the sensitivity of the method to 2 and 1 $mg.L^{-1}$, respectively (Newlands et al. 1979).

XAD macroreticular resins are particularly useful for the extraction and concentration of residues of aminocarb and its metabolites in water. Brun and MacDonald (1980) showed that, at pH 7, the recovery of AC, MAA and aminocarb was > 86% (0.2 $mg.L^{-1}$) and that of AA and MAA was 67% and 32% respectively. Sundaram et al. (1979) used XAD-2 resin as part of a general method for the recovery of carbamates, including aminocarb, from water. Between pH 5 and 7.5, the recovery was >90% (0.5 $mg.L^{-1}$) and 98% from natural water (0.01 $mg.L^{-1}$). These resins offer a facile method of extraction and concentration of insecticides from water.

2.4.2.2 Cleanup

The basic character of the amino moiety of aminocarb facilitates the cleanup of crude extracts. Aqueous extracts are acidified, extracted with solvents to remove lipophilic coextractants, then the aqueous solution basified to pH 6.5 - 7 to liberate the free carbamate. Care has to be taken in adjusting the pH since carbamates hydrolyze rapidly in alkaline solution. A saturated solution of sodium bicarbonate is recommended, followed by immediate extraction of aminocarb with methylene chloride or ethyl acetate (Table 2-2).

The coagulation technique of Johnson (1964), with 0.15% NH_4Cl in 0.30% H_3PO_4, was used by Mamarbachi (1978) and Szeto and Sundaram (1980) for cleanup of soil, sediment, foliage and fish samples.

2.4.2.3 Detection

Wheeler and Strother (1969) first reported on the thermal degradation of aminocarb to its phenol on GC columns. Mamarbachi (1978) showed it was dependent on the particular column substrate and temperature (Figure 2-2). Perfluoroacylation of aminocarb has been used to overcome this problem (Sundaram et al. 1976). The availability of deactivated GC column packings, such as the Ultraphase® supports, now enables routine GC analysis of intact aminocarb to be carried out at temperatures up to 180°C with <3% decomposition. Levesque and Mallet (1980) have reported on the GC retention times and detection limit of aminocarb and seven derivatives. A GC chromatogram of A[α], AC, MAA, FA and C (Weinberger et al. 1980) is shown in Figure 2-3.

[α] Abbreviations are defined inside the back cover.

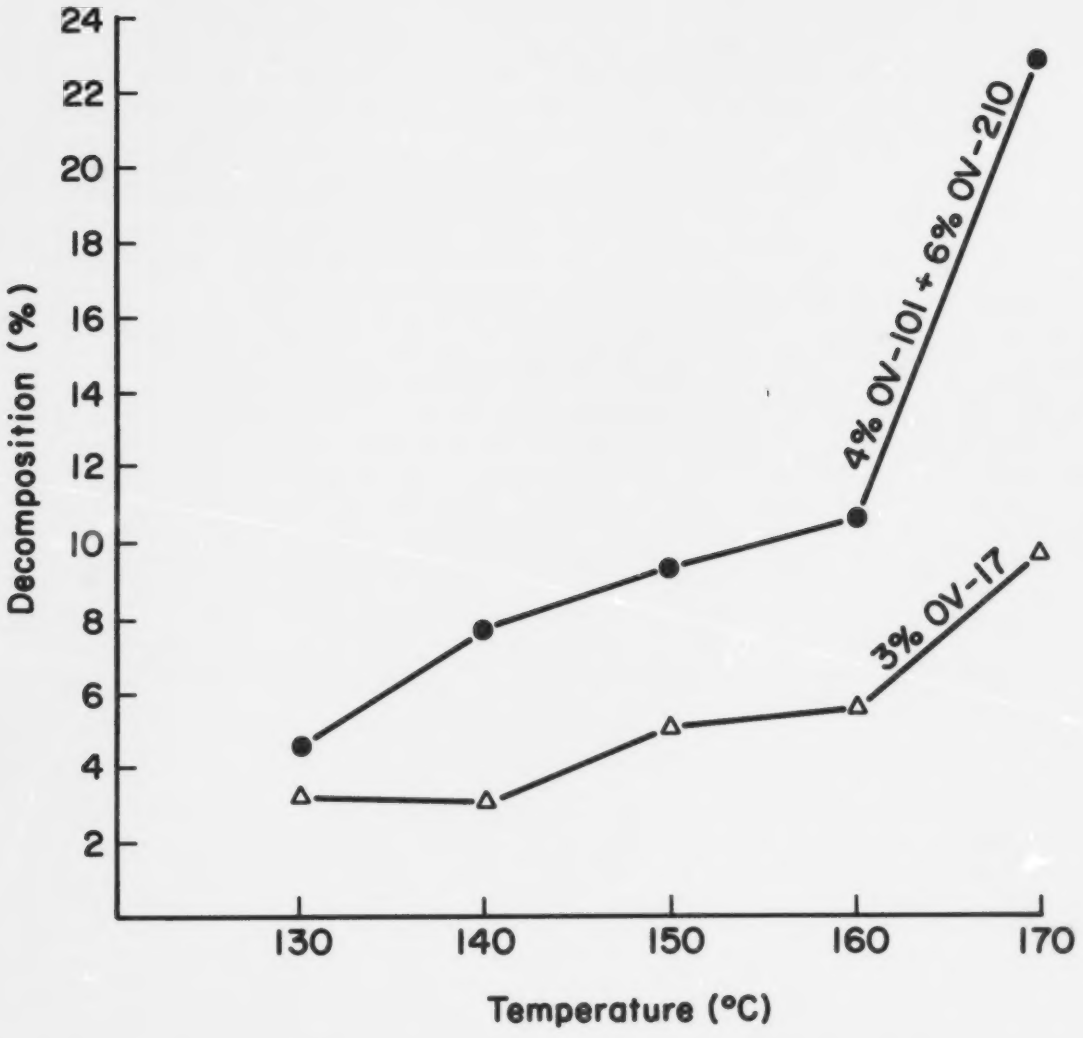

Figure 2-2. Decomposition of aminocarb on various GC column substrates versus temperature (Mamarbachi 1978).

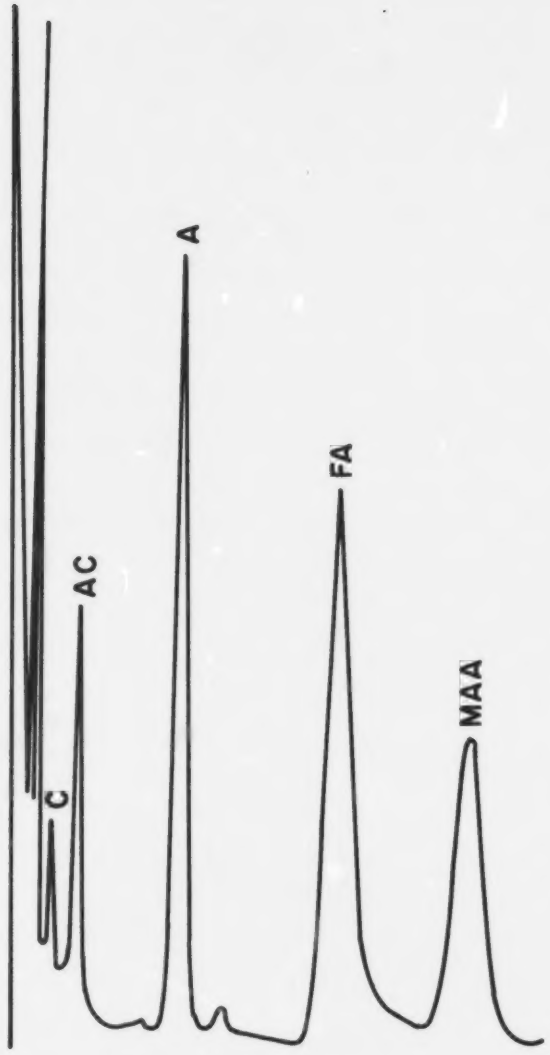

Figure 2-3. GC chromatogram of A, AC, MAA, FA and C (see inside back cover) (Weinberger et al. 1980).

Instrument: Hewlett-Packard model 5880 GC
Detector: Nitrogen-phosphorus
Column: 2 ft x 1/8" 3% OV17 on Ultra-Bond 20M (100/120 mesh)
Temperatures: oven 170°C, injection port 170°C, detector 250°C
Flow rates: Carrier (N_2) 34 $mL.min^{-1}$, H_2 3.1 $mL.min^{-1}$, air 59 $mL.min^{-1}$

The first selective GC detector used for aminocarb analysis was the Hall electrolytic conductivity detector in the nitrogen mode (Brun and MacDonald 1978; Sundaram et al. 1978). Lawrence (1976) experimented with the use of this detector in the halogen mode using the perfluoro derivatives of aminocarb. However, current analytical procedures generally employ the heated bead thermionic detector. It is more sensitive to aminocarb than is the Hall detector by a factor of at least 10, with a minimum detectable amount of 50 pg. The sensitivity and ease of use of the thermionic detector make it the detector of choice for GC procedure.

HPLC procedures have also been used for analysis of aminocarb and its derivatives in water. Brun and MacDonald (1978) found that the reverse phase LiChrosorb RP-2 (10 μm) gave better separation than LiChrosorb RP-8 or HC-ODS/Sil-X. Aminocarb phenol chromatographed poorly in acetonitrile:water, 1:4, and it was necessary to use buffers (Borax:NaOH, pH 7.4 or phosphate, pH 7.9) to improve peak shape and sensitivity. Both UV (254 nm) and fluorescence (Excit. 248 nm) detectors gave a linear response for aminocarb with detection limits of 0.5 $\mu g.L^{-1}$ and 0.05 $\mu g.L^{-1}$ respectively (S/N, 2:1), for a 1 L sample size. Although the electrochemical detector (ED) has a similar sensitivity to that of the UV detector, its use has only been reported for the analysis of formulations. It would be expected that its selectivity offers some advantage for use in residue procedures.

Lanouette and Pike (1980) compared the performance of the ED and UV detector for aminocarb. The minimum detectable amount (S/N, 2:1) was 3 ng for both detectors, but the linear range for the UV was greater, 10^3 (10 ng - 10 μg) compared with 10^2 for the ED. The sensitivity of the ED decreased with repeated analysis. This fact together with the better linear range of the UV detector indicates the latter to be better for formulation analysis.

Only one procedure for the analysis of aminocarb in mammalian urine has been described (Everett 1965). This procedure involves hydrolyzing putative conjugates of C[α], extracting with chloroform, and reacting it with 4-aminoantipyrene. The resulting compound can be assayed through a 470 nm filter. This test proves adequate to detect C at concentrations of 1-1000 $mg.L^{-1}$. However, the specificity of the coupling agent, 4-aminoantipyrene, is not well defined and, almost certainly, modern chromatographic techniques could be used to replace some of the slow solvent extractions used by Everett.

2.4.3 STABILITY OF AMINOCARB IN ORGANIC SOLVENTS

In the non-chlorinated organic solvents, acetonitrile, benzene, cyclohexane, ethyleneglycol monomethyl ether, n-hexane, toluene

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[α] Abbreviations are defined inside the back cover.

or xylene, carbonyl-^{14}C-aminocarb (150 $\mu g.mL^{-1}$) was stable for ten days (Abdel-Wahab 1971). The solutions, in sealed glass tubes, were exposed to laboratory light at room temperature. In contrast, solutions in acetone were appreciably degraded (~ 5%) and solutions in chlorinated solvents, i.e. chloroform, carbon tetrachloride or methylene chloride, were extensively degraded (30 to 60% decrease in starting material). A multiplicity of products was observed. Between three and nine active products were detected when the tube contents were chromatographed on silica gel thin layer plates. Although the chemical identity of the products was not determined, the extensive degradation indicates that samples for residue analysis should not be stored in chlorinated solvents or in acetone.

In general, the stability of aminocarb analogs varies directly with the degree of substitution of the aryl amino group. The same caution regarding the choice of storage solvents will also apply to aminocarb transformation products.

2.4.4 GOOD LABORATORY PRACTICE

A priori, there will be some inherent variability in the results obtained by any analytical procedure. This variability will be dependent on concentration as documented by Horowitz (1981) using data from the Association of Official Analytical Chemists (AOAC) interlaboratory studies (Figure 2-4). This figure indicates that the error associated with the analysis of residues increases exponentially as their concentrations decreases. There are four major sources of variability in pesticide residue analysis: sampling, method, analysis and misinterpretation of analytical data. In general, at the $mg.kg^{-1}$ level, sampling is the main source of variability with a coefficient of variation >20%. At and below $\mu g.kg^{-1}$ levels, the other factors are equally important. Since the analytical procedures for aminocarb in milk, sediment and water have detection limits in this range (Table 2-2), it is essential that good laboratory practices (GLP) be observed. Thus, the need for confirmation of positive GC responses at the $\mu g.kg^{-1}$ level is essential.

In Canada, the laboratories involved in the analysis of aminocarb are associated with government, universities and industry. The analytical expertise in these laboratories varies considerably; strict observation of GLP is necessary if meaningful data are to be developed by research as well as routine laboratories. Carl (1978) has discussed the effects of using internal laboratory controls on the precision and accuracy of data for organochlorine compounds. His comments are equally valid for other compounds.

In addition, interlaboratory studies should be carried out between all laboratories engaged in aminocarb residue analysis with emphasis on matrices found in the forest environment. Although the trend is toward the use of GC/NPD methods for the quantitation of aminocarb residues, much data have been generated by HPLC methods with

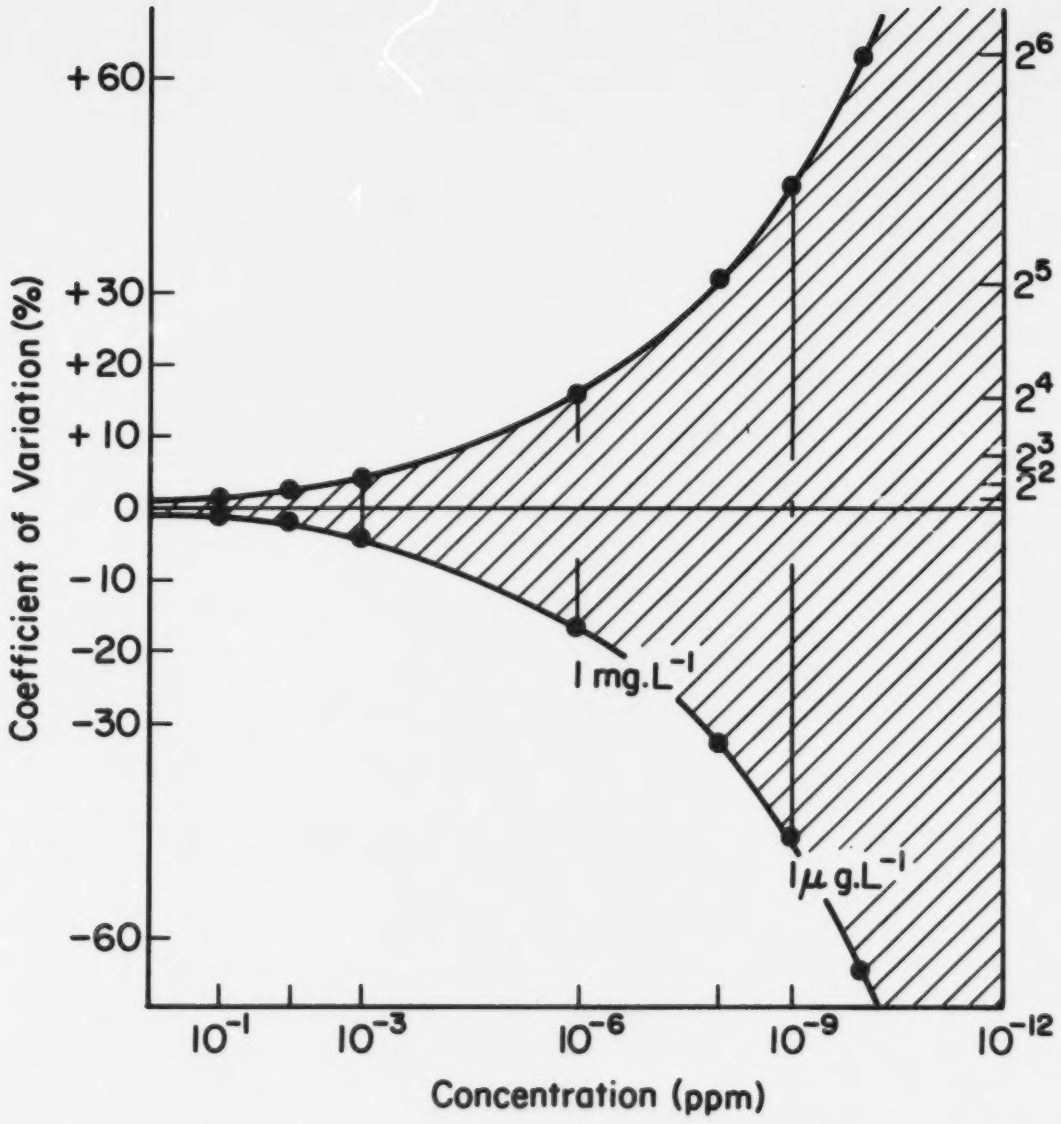


Figure 2-4. Interlaboratory coefficient of variation as a function of concentration (Horowitz 1981).

various detectors. In order to ensure that the data generated in different laboratories using different methods and equipment are comparable, these studies are necessary.

2.5 CHEMICAL DEGRADATION OF AMINOCARB

2.5.1 HYDROLYSIS

The term hydrolysis as used below is considered to be the cleavage of the carbamate moiety of aminocarb to give 4-(dimethylamino)-3-methylphenol and methyl-carbamic acid, which rapidly degrades further to carbon dioxide and methylamine (Patel 1978).

In aqueous systems the stability of aminocarb increases as the temperature and the pH decrease (Murphy et al. 1975b). Abdel-Wahab et al. (1966) found that the half-life of ^{14}C-carbonyl-labelled aminocarb in pH 9.3 veronal buffer (ionic strength = 0.1 F) at 25°C was 4 h. They measured hydrolysis by the amount of radioactivity extracted into diethyl ether (which excluded any $^{14}CO_2$ produced upon hydrolysis). The authors did not state the kinetic order of the reaction or whether the reaction was carried out in the dark.

Murphy et al. (1975b) also examined the fate of (carbonyl-^{14}C) aminocarb at 10 mg.L^{-1} in 0.2 M phosphate buffers (pH 5.0, 7.0 or 9.0) in the dark and at 5, 20 or 50°C. Hydrolysis appeared to be the dominant reaction at all three pH values. At 5°C, essentially no change was observed over a 28 day period, but at higher temperatures some decomposition was evident. Estimated half-lives for the substrate in each solution at 20°C and at 50°C are contained in Table 2-3. The ether-extractable portion consisted mainly of aminocarb, except in the 50°C runs, where after 4 days the N-demethylated aminocarb accounted for 30% and 50% of the organo-soluble activity at pH 7.0 and pH 9.0, respectively. However, in both cases only small amounts of the initial activity (< 5%) were recovered by extraction.

A more detailed study confirmed these earlier observations. Using (ring 1-^{14}C) aminocarb at 1 or 10 mg.L^{-1} in three phosphate buffers (pH 4.4, 7.0 and 9.3) Tessier et al. (1978) studied stability in the dark as a function of two storage temperatures (30 and 40°C). Estimated half-lives for these storage conditions are given in Table 2-3. Under these conditions decomposition appears to be essentially independent of concentration. At pH 4.4, virtually all of the activity was organo-soluble (ethyl acetate) after 28 days and the chemical composition of this fraction was unchanged from time zero. At pH 7.0, the stability was considerably decreased and variable amounts of radiolabelled products were extracted after 28 days. This organo-soluble fraction of the total recoverable activity (~ 68% for the 30°C studies) was reduced to approximately 45% at the higher storage temperature. Aminocarb was a relatively minor component of this

Table 2-3. Estimated half-lives (d) for aminocarb in aqueous phosphate buffers as a function of storage temperature in the dark (Murphy et al. 1975b; Tessier et al. 1978).

pH	$t_{\frac{1}{2}}$(d) Storage T°C 20°	50°	pH	$t_{\frac{1}{2}}$(d) Storage T°C 30°	40°
5.0	90.2	2.8	4.4	151[α] 211	128[α] 130
7.0	28.5	0.6	7.0	10[α] 11	5[α] 8
9.0	5.7	0.2	9.3	0.6[α] 0.6	0.2[α] 0.2

[α] Solution was 1 mg.L^{-1}. In all other cases it was 10 mg.L^{-1}.

fraction (~16%) with less C[α] and small amounts (<3%) of MAA. Considerable amounts of polar material remained at the origin of the eluted TLC plates (silica gel; benzene, acetonitrile, hexane (1:1:1) or diethylether, hexane, ethanol (77:20:3)), and there were several unidentified products.

At pH 9.3, the aminocarb concentration was negligible after four days. MAA was present during the first seven days and FC was observed in small amounts (<2%) through day 28. Radiolabelled products present in the aqueous fraction remained at the origin when this mixture was chromatographed by TLC.

In these studies, dissolved oxygen concentration averaged 10 $mg.L^{-1}$. The multiplicity of products indicate that the half-lives are best regarded as dissipation rates, reflecting a combination of hydrolytic and oxidative processes with the former predominating.

In a more recent study, Weinberger et al. (1980) investigated the hydrolytic fate of (^{14}C-ring) aminocarb in lake water (pH 7.4 to 7.5, specific conductance 61 ± 2 μS(siemens).cm^{-3}). A formulated mixture (aminocarb:nonyl phenol: 585 oil in the ratio 2:4:3) was prepared by dissolving "Matacil 1.8D" and labelled substrate in lake water to give a concentration of 10 $mg.L^{-1}$ aminocarb. The formulated and non-formulated solutions were then stored, in the dark, at 25, 33 or 50°C, and sampled regularly. The calculated half-lives in lake and distilled water are included in Table 2-4. Degradation was rapid at 50°C and the degradation followed first-order kinetics. After 13 h, only 70% of the substrate could be extracted with ethyl acetate. The organo-soluble fraction contained approximately 20% unchanged aminocarb with the remainder mostly C, some AC and an unknown compound which remained at the origin when this fraction was chromatographed (silica gel in 19:1, chloroform:ethanol). Interestingly, considerably more C and less polar material (organo-insoluble) was observed with the non-formulated than with the formulated substrate. An Arrhenius plot for formulated aminocarb in lake water suggested a half-life ($t_{½}$) value = (456 T^{-1} - 8.55) d where T is the temperature in °C. (Activation energy = 3.8 $kJ.°K^{-1}.mol^{-1}$, ln A = 5.93).

The active role played by microorganisms present in natural lake waters was evidenced by a comparison of ^{14}C distributions resulting from formulated substrate in distilled water or in natural lake water. In the former system, after 35 h only 3% of the total recovered activity was organo-insoluble, whereas in natural lake waters, 88% of the recovered activity was organo-insoluble. A multiplicity of products, as yet unidentified, was present in both the polar and nonpolar fractions.

[α] Abbreviatons are defined inside the back cover.

Table 2-4. Estimated half-lives ($t_{\frac{1}{2}}$) for aminocarb (10 $mg.L^{-1}$) in distilled or lake water as a function of storage temperature in the dark (Weinberger et al. 1980).

Water	°C	$t_{\frac{1}{2}}$ (d) Formulated	Nonformulated
Lake	50	0.20	0.16
Lake	33	6.0	-
Lake	25	9.3[α]	10.5
Distilled	25	20.6	-

[α] Does not fit first-order kinetics well; $t_{\frac{1}{2}}$ is a visual estimate.

2.5.2 OXIDATION

Balba and Saha (1974) employed an *in vitro* oxidative system (Udenfriend *et al.* 1954) to study the oxidation of (aryl N-methyl-^{14}C)-aminocarb. After a reaction time of two hours at least twelve products were detected by thin layer chromatography. These included two N-demethylated products (AA and MAA), C and the carbamate N-hydroxymethyl derivative, HMA. Evidence was presented which suggested that hydroxylation of the aromatic ring (a hydroxylated isomer of MHA) had occurred. Unreacted aminocarb accounted for 48% and N-demethylaminocarb for 30% of the total activity; the other products accounted for less than 3.5% of the total activity.

No transformation products corresponding to oxidation of the aryl methyl group or further oxidation of the carbamate N-methyl group have been reported to date, unlike the case of fenitrothion, where these processes constitute the main oxidative degradation route (Miyamoto *et al.* 1968).

In Figure 2-5 a hypothetical oxidative decomposition scheme is proposed for aminocarb. Each functional group is oxidized sequentially, resulting ultimately in a p-amino group, a m-carboxyl and an unsubstituted carbamate. Depending on the circumstances of degradation, any one route may proceed more rapidly than the other two. Thus, "cross-products" which contain two or more partially oxidized functional groups seem likely. Little is known concerning the stability of several of these products or their toxicity. A multiplicity of oxidation products can be anticipated because each of these intermediates can be hydrolyzed to liberate the corresponding phenols.

2.5.3 PHOTOLYSIS

In laboratory studies it is important to use conditions which approximate natural sunlight, particularly with respect to the wavelength and intensity of irradiation. Most of the photolytically active sunlight at the earth's surface falls into the 290-450 nm range. Mercury lamps which are not equipped with a borosilicate glass filter emit most of their radiation at 254 nm. This high energy radiation may produce photoproducts of aminocarb that sunlight would not produce.

2.5.3.1 In Solution

Several groups of investigators have studied the photolytic stability of aminocarb in or on a variety of matrices. Addison *et al.* (1974) have reported that C is the major product when aminocarb in aerated or degassed ethanol or cyclohexane is irradiated with light of 300 nm (high pressure Xenon-mercury lamp). Only traces of other products were observed. They pointed out that the phenol (C) would be expected on the basis of a photo-Fries mechanism (Addison 1978). Yields

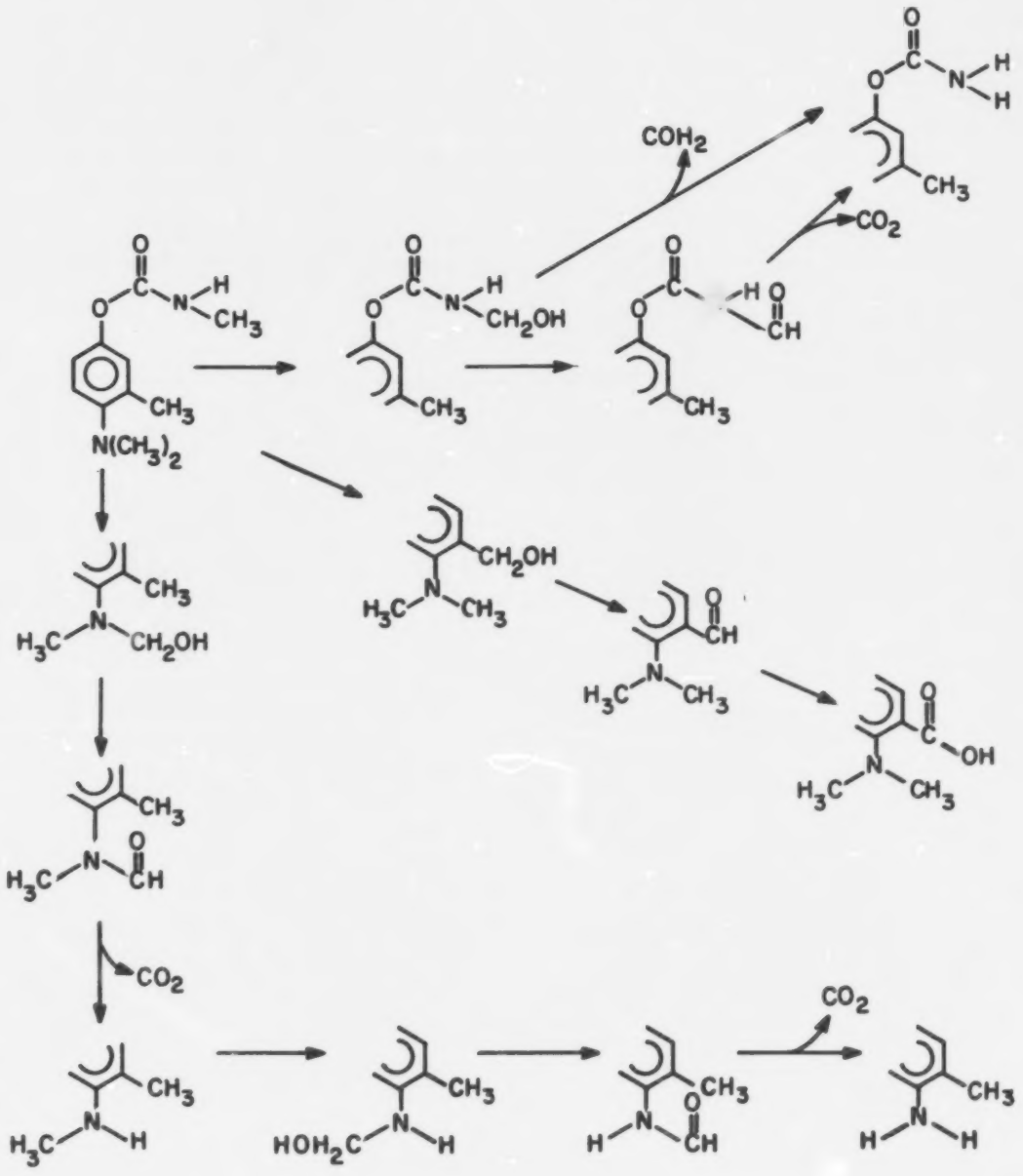


Figure 2-5. Hypothetical oxidative decomposition scheme for aminocarb.

of C were 11% after 16 h irradiation in aerated ethanol versus 8% after 15 h irradiation in degassed ethanol.

Crosby et al. (1965) combined TLC with an assay for acetylcholinesterase to demonstrate that aminocarb (in ethanol or hexane) was transformed in 3 h to at least five cholinesterase inhibitors when irradiated with ultraviolet light (254 nm). Although the chromatographic behavior of the products was reported, their chemical identity was not determined.

In phosphate buffered water (pH 4.9, ionic strength = 0.2 F) the half-life of (ring 1-^{14}C) aminocarb (5 mg.L^{-1}) was estimated to be 10 d when it was exposed to a Hanovia high pressure quartz mercury vapor lamp (Mulkey et al. 1978). The lamp intensity, incident on the sample, was determined to be 0.34 watts using an uranyloxalate actinometer. After 30 d exposure, only 48% of the activity could be extracted with ethyl acetate. A further 22% was present in the aqueous fraction. The only products positively identified were MAA and unreacted aminocarb which accounted for one-third of the activity in the organic extracts. The dissipation rates approximated those predicted for first-order kinetics.

The half-life was reduced to 1.5 d with 2% acetone added as a sensitizer. After 11 d exposure, activity in the ethyl acetate extracts accounted for 65% of the initial value, but no aminocarb or MAA product could be detected. A further 24% was present in the aqueous fraction.

The environmental degradation should be investigated by determining the sunlight photolysis of aminocarb dissolved in water. None of the above three studies has done this. Crosby et al. (1965) used an antichlolinesterase product assay, which is unsuitable for the phenol hydrolysis product. Mulkey et al. (1978) did not employ a dark control, yet they earlier reported significant oxidative/hydrolytic degradation of aminocarb held for the same period of time in the dark, under otherwise practically identical conditions.

2.5.3.2 On Surfaces

Abdel-Wahab et al. (1966) and Abdel-Wahab and Casida (1967) tentatively identified four (of 11 observed) sunlight photoproducts on bean leaves as MAA (the major product), MFA, FA and AA. Aminocarb was extensively degraded after three days of sunlight irradiation. Sequence studies on thin layer chromatographic plates using ultraviolet light (254 nm) showed that aminocarb gives rise to the MAA and MFA analogs; the MAA derivative further degraded to the AA and FA analogs.

Augenstein et al. (1978) studied the Hg lamp photolysis of (ring-^{14}C) aminocarb applied to a sandy loam forest soil, over a period of eight days. About 33% of the applied radioactivity was volatilized

by the heat from the lamp, and 50% was bound to the soil. The photolytic half-life of aminocarb on the soil was 4.6 h. No photoproduct, either identified or unidentified, accounted for more than 10% of the initial applied radioactivity. Five of the eight photoproducts were identified as MFA, MAA, FA, AA and FC.

In contrast to the claim of Addison et al. (1974) that C is the major product, most of the other studies indicate that the main reaction is oxidation of the dimethylamino ring substituent; this point should be resolved.

2.5.3.3 Vapor Phase

Addison (1981a) reported a $t_{\frac{1}{2}}$ = 38 ± 2 min for the photolysis of aminocarb in the vapor phase in the laboratory. Products were not identified. He speculated that extensive photolysis might occur during spray drift.

2.6 METABOLISM OF AMINOCARB

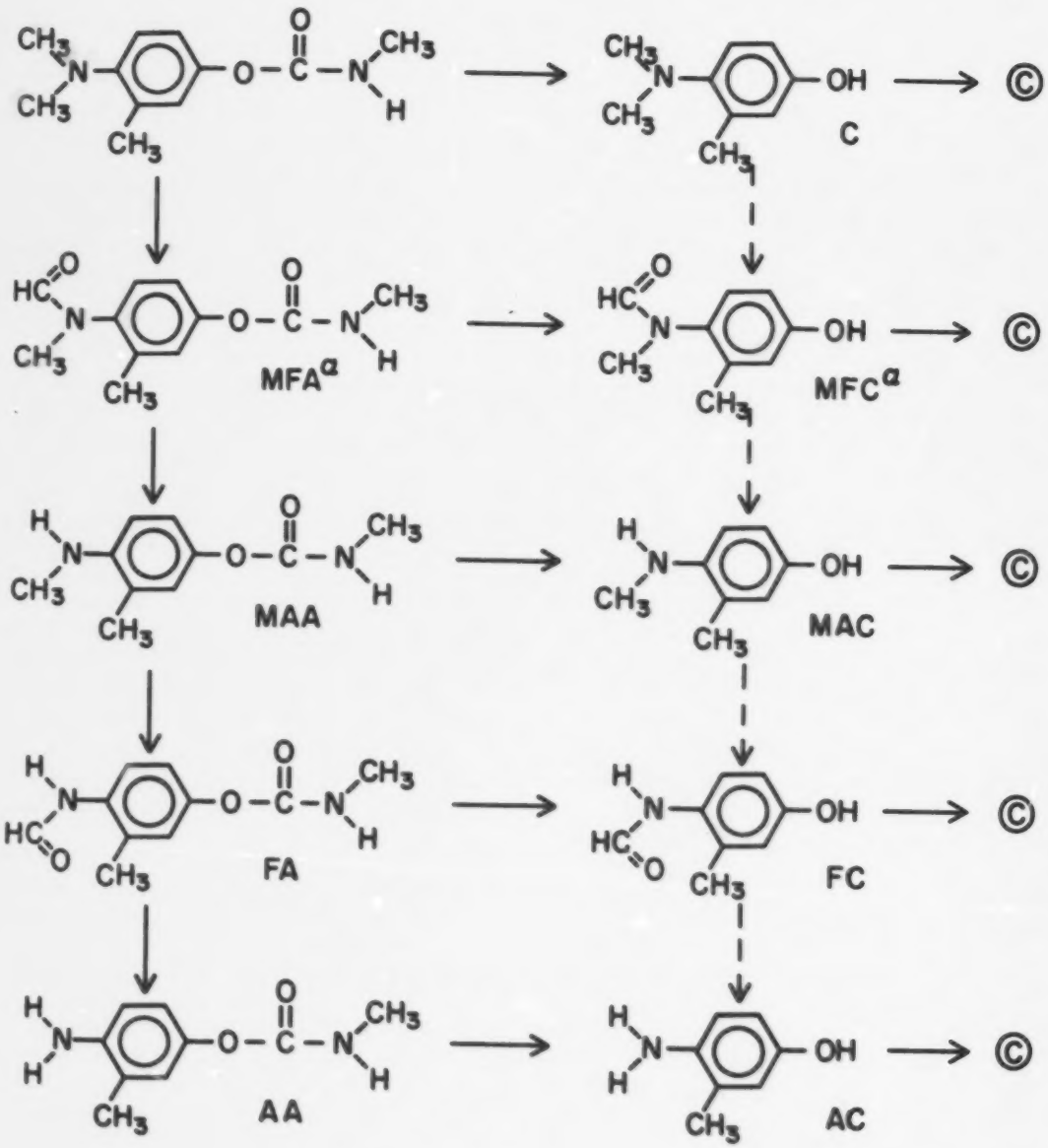
Most vertebrates and invertebrates can enzymatically degrade aminocarb. Metabolic degradation has been studied both in vivo and in vitro. In the former, hydrolysis of the carbamate linkage is the predominant reaction, whereas it is a minor reaction in the latter. The principal fate of aminocarb in vitro involves oxidative demethylation of the dimethylamino group (Oonnithan and Casida 1968) and to a lesser extent the methylamino group of the carbamate moiety (Strother 1972).

2.6.1 IN VITRO ENZYME SYSTEMS

Aminocarb is metabolized by an $NADPH_2$ enzyme complex, such as that found in human and rat livers (Strother 1970, 1972; Oonnithan and Casida 1966, 1968) and the abdomens of resistant houseflies (Tsukamoto and Casida 1967). Radiolabelled substrate was converted by a housefly homogenate to MAA, AA and a small amount of FA (Tsukamoto and Casida 1967).

Rat liver microsomal fraction $NADPH_2$ systems yielded at least nine metabolites of C^{14} aminocarb and at least one additional metabolite was detected in human liver (Strother 1970). In rat liver, the major transformation products were MAA, HMA and AA, accounting for approximately 25%, 19% and 3% respectively, of the original aminocarb. The same products were identified in human liver but they represented only 4%, 1% and 3% respectively, of the original aminocarb (Strother 1972).

Presumably oxidation of the carbamate amide methyl group can occur with any of the ring-amino oxidation products (Figure 2-6), but



[α] These metabolites not actually detected.

Figure 2-6. A proposed scheme for the metabolism of aminocarb in swine (based on Shaw 1978). Ⓒ indicates conjugated compounds.

the HMA metabolite of aminocarb itself is the only one that has been demonstrated (Oonnithan and Casida 1968). This compound probably represents the first product of the oxidative demethylation of the carbamate nitrogen (although the demethylation product has not been identified among the excreted metabolites). Other possible oxidative reactions are ring hydroxylation and oxidation of the ring methyl group, but with aminocarb these two possibilities have been neither demonstrated nor effectively ruled out (Oonnithan and Casida 1968). Although MFC and FC were not actually detected in aminocarb-liver incubates, a Zectran metabolite analogous to MFA was detected when Zectran, which differs from aminocarb only in possessing a methyl group in ring position 5, was incubated. Hydrolysis of the carbamate ester bond is not important in liver homogenates (Strother 1972) although, in the whole mammal, it is a major reaction (Section 2.6.2).

In the rat liver incubations, aminocarb proved the most resistant to metabolic degradation of nine carbamate pesticides tested (Oonnithan and Casida 1968). Human liver preparations were even less effective than rat liver fractions in metabolizing it (Strother 1970, 1972). At the end of the incubation, about 78% of the aminocarb remained intact in the preparations of human liver, whereas only 33% (or 20% in the study by Oonnithan and Casida 1968) escaped alteration in rat liver homogenates (Strother 1970, 1972).

All the studies described were qualitative in that not all the metabolites were identified nor were the rates of formation and mass balance reported.

Aminocarb is also rapidly degraded by horseradish peroxidase to yield products which are mainly insoluble in ether (Kuhr and Casida 1967). Among the ether soluble metabolites were MAA and the AA. In this case HMA was not detected.

2.6.2 METABOLISM IN ANIMALS

Krishna and Casida (1966) administered carbonyl-^{14}C-aminocarb intraperitoneally to rats and found, after 48 h, that 67% of the radioactivity was expired as $^{14}CO_2$, 25% was excreted in the urine, 3.8% in the feces and the remainder was left in the body, mainly in the blood. The relatively large amounts of radioactivity expired as $^{14}CO_2$ indicate that, *in vivo*, hydrolysis of the carbamate ester bond is the major degradative pathway.

Shaw (1978) found that after a single oral dose (0.5 mg.kg^{-1}) of ^{14}C-aminocarb was fed to miniature male and female Hoxmel swine, essentially all of the radioactivity was excreted in the urine within 24 h and 10% of the radioactivity was excreted in the unconjugated form. However, 87% of the initial dose was rendered organo-soluble by acid hydrolysis. Conjugates of C and MAC were the major metabolites, again indicating the importance of hydrolysis *in vivo*. In the case of MAC, it is not known whether hydrolysis of aminocarb preceded oxidation or vice

versa. Non-conjugated material in the original organic extract included the corresponding intact carbamates as well as the p-formamide analogues. Metabolites based on the oxidation of the N-methyl amide (e.g. HMA) were not detected in the urine or tissues of pigs. A proposed scheme for the metabolism of aminocarb in swine is shown in Figure 2-6.

Only the kidney and the liver had residues greater than 0.1 $mg.kg^{-1}$ when the animals were dosed daily for five days (0.5 $mg.kg\text{-}BW^{-1}$) and sacrificed 45 min after the last dose. A small amount of the total label in these organs was organo-soluble; however, prior acid hydrolysis greatly increased recovery. The spectrum of products was similar to that of urine (Shaw 1978).

In the pig, the phenolic metabolites of aminocarb appear to be extensively conjugated to form highly polar, water-soluble compounds that cannot be extracted by such organic solvents as ethyl acetate or n-butanol.

The extensive conjugation of phenolic metabolites of aminocarb by miniature pigs is probably not the pattern in all mammals. For example, Williams et al. (1964) were able to recover 92% of the radioactivity in the urine of Zectran[α]-dosed dogs by extracting the alkaline urine (pH 8) seven times with n-butanol; the same treatment of urine from aminocarb-treated pigs yields only 4% of the administered dose (Shaw 1978). This contrast probably reflects less a difference between aminocarb and closely related Zectran[α] than a difference between pigs and dogs in their capacities to conjugate phenols. What pattern fits man is not clear, but Everett (1965) reported almost complete extraction of aminocarb metabolites in human urine after intense acid hydrolysis.

2.6.2.1 Absence of Liver Microsomal Enzyme Induction

Evidence summarized above establishes that aminocarb is metabolized in vivo by a group of liver microsomal enzymes which are commonly referred to as the "mixed function oxidase system". Some, but not all, exogenous substances that behave as substrates for this oxidase system are able to stimulate the liver into synthesizing larger than normal amounts of these microsomal enzymes. In this way these substances promote their own degradation as well as that of many other exogenous chemicals. This induction of enzyme protein synthesis generally requires repeated or continuous exposure to the inducing chemical over a period of several days.

To investigate the capacity of aminocarb to function as an inducer, DuBois and Kinoshita (1965) injected rats intraperitoneally

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[α] Mexacarbate.

with 4 mg.kg-BW^{-1} aminocarb daily for 5 d, which is a high but tolerable dose (DuBois and Kinoshita 1962). Other groups of rats received daily injections of known inducers of liver microsomal enzymes: DDT, chlordane, toxaphene (each at 10 mg.kg-BW^{-1} daily) and phenobarbital (at 50 mg.kg-BW^{-1} daily). Twenty-four hours after the fifth injections, the rats were sacrificed and the livers removed. Liver homogenates were tested for their ability to catalyze the conversion of O-ethyl O-p-nitrophenyl phenylphosphonothioate (EPN) to p-nitrophenol. In livers from rats pretreated with DDT, chlordane, toxaphene or phenobarbital, this enzymatic reaction was 2 to 4 times faster than in livers of control animals. In aminocarb-pretreated rats, the reaction rate was the same as in the controls.

The conclusion that aminocarb is unable to induce at least one microsomal enzyme in rats (DuBois and Kinoshita 1965) appears to be valid, but it would have been more appropriate to have used one of the oxidative microsomal enzyme reactions rather than a phosphoesterase as the test system.

2.6.2.2 Absorption, Distribution and Excretion in Laboratory Mammals

No extensive pharmacokinetic description of aminocarb is available. Only two relevant reports were located; (1) a comparative study involving 15 different ^{14}C-labelled carbamate pesticides (including aminocarb) administered intraperitoneally to white rats in a single dose of about 1.5 mg.kg-BW^{-1} (Krishna and Casida 1966); (2) the previously mentioned study of aminocarb in two miniature pigs involving a single oral dose of 0.5 mg.kg^{-1} and five later daily doses of 0.26 mg.kg^{-1} (Shaw 1978). In the rat study the ^{14}C label was located on the carbonyl carbon, and so the distribution of radioactivity reflected the distribution of the carbamate portion of the aminocarb molecule and its metabolites. In the test on pigs the ^{14}C label was on the ring, and so its distribution reflected that of the phenolic portion of the molecule and its metabolites.

Absorption of aminocarb was rapid from the peritoneal cavity (rat) and from the gastrointestinal tract (pig). In pigs, the blood level of radioactivity peaked within the first hour. As noted before, extensive hydrolysis of the ester bond occurred in both species. Both the carbamic acid moiety and the phenolic moiety were excreted rapidly. The former appeared as $^{14}CO_2$ in expired air to the extent of 67% of the administered dose of radiocarbon, more than half within the first 4 h (rats). The phenolic moiety appeared as various metabolites in voided urine to the extent of 70% to 83% of the administered dose (93% to 95% during the period of multiple daily dosing) within 24 h (pigs). In rats, 22.9% and 1.7% of the administered carbonyl-^{14}C was excreted in urine in the first and second 24-hour periods respectively. Fecal excretion of ^{14}C accounted for less than 4% of the administered dose in rats and less than 2% in pigs.

The carbonyl-^{14}C label was retained in rat tissues to a considerably larger extent than the ring-^{14}C label in pig tissues. Thus about 8.8% of the original dose was present in rat tissues and organs after 48 h. In contrast, ^{14}C concentrations in pig tissues were 2 to 3 orders of magnitude lower, even though the pigs were sacrificied only 45 min after the last 5 daily doses. Relative concentrations of the two labels, however, were not greatly dissimilar. On the basis of a normalized ^{14}C concentration of 1.0 in heart, the following values were reported in pig organs: kidneys 13, liver 4, fat 1, muscle 0.6 and brain 0.37. Corresponding concentrations of the ^{14}C label in rat organs were 1, 1.3, 0.25, 0.51 and 0.52. Additional values in rats included spleen 1.5, lungs 0.91, bone 0.57, blood cells 3.1 and plasma 0.35. The higher ^{14}C concentration in blood cells than in plasma was noted with all of the carbonyl-^{14}C-labelled methylcarbamates tested in rats.

2.6.3 METABOLISM IN BIRDS

Lamb et al. (1978) have studied the ability of bobwhite quail to metabolize and eliminate ring-C^{14}-aminocarb. The birds were given feed containing 10 or 50 mg.kg-diet^{-1} of aminocarb for fourteen days and then placed on an untreated diet for an additional fourteen days. The majority of the ^{14}C was eliminated in the feces during the treatment period. The concentration of ^{14}C residues in any tissue (breast muscle, liver or mesenteric fat) was less than 10% of the dietary levels after this time. This concentration was reduced to <1% at the end of the withdrawal period. The nature of the metabolites was not investigated.

2.6.4 METABOLISM IN PLANTS

On the surface of growing bean leaves, carbonyl-^{14}C-aminocarb was rapidly degraded to eight or more products, the sum of which reached a maximum after 24 h if the plants were placed outside (Abdel-Wahab et al. 1966). If the compound was injected into the stem of these plants, only 5% of the original aminocarb remained after 24 h. One quarter of the label was lost, presumably by respiration, and a further 59% could not be extracted from the plant material. The identity of the degradation products in the organo-soluble fraction (5% of initial activity) was established by cochromatography on TLC. These included the FA, MFA, AA and MAA analogs of the parent carbamate. The method of analysis was not, however, designed to reveal phenolic hydrolysis products or their conjugates. The relative rates of dissipation were obtained by estimating the incubation times required to reduce the initial extraction recoveries of labelled compounds by half. For aminocarb, the 50% recovery time was estimated to be 2.4 h and for total organo-solubles 3.6 h. From an aqueous solution buffered to pH 9.3 the incubation time, as defined above, was estimated to be 4.0 h.

The water-soluble metabolites from the administration of carbonyl-^{14}C-aminocarb to intact bean plants were studied in a subsequent report by Kuhr and Casida (1967). Treatment of this fraction

(8% initial dose) with β-glucosidase released five aglycones, none of which inhibited cholinesterase.

Nagel et al. (1978) sprayed (ring-^{14}C)-aminocarb on Colorado blue spruce trees and the foliage was sampled over 23 d. Aminocarb appeared to be 64% dissipated during this period. There were no significant amounts of volatiles formed. The MAA analog was the only metabolite identified; of the several unidentified compounds none accounted for more than 10% of the radioactive residue. After 28 d, the radioactivity was distributed in the following manner: 36% aminocarb, 4% MAA, 4% bound, 23% in the aqueous extract, 12% in the ether extract, 2% in the benzene extract and 19% lost.

In general, metabolism of aminocarb in plants appears to be by oxidation, although the experimental data are not conclusive since many products were not identified and the analytical methods used would sometimes not have detected phenolic metabolites. Aminocarb is degraded fairly quickly in animals and plants, but less rapidly when sprayed on spruce foliage.

It should also be noted that some of the oxidative metabolites of aminocarb that possess an intact carbamate moiety appear to be more toxic than the parent compound (Mulkey et al. 1978). Several transformation products remain unidentified and their toxicities are unknown. In general, it may be incorrect to associate the degradation of parent compounds with diminished hazard if more toxic stable products can result.

2.7 PERSISTENCE AND RESIDUES IN ENVIRONMENTAL COMPARTMENTS

2.7.1 AMINOCARB

Table 2-5 summarizes data on the first-half-lives ($t_{\frac{1}{2}}$)[α] of aminocarb observed in a variety of media. Data are included from studies in which several chemical processes may be contributing to its disappearance. In some situations, the apparent overall loss of aminocarb may be associated with "growth dilution", a decrease in the concentration simply because of an increase in the population or mass of plants or animals. Also, half-lives may be affected by the total dynamics of a system, especially in situations where input of aminocarb to a specific compartment is continuous for some time after spraying, e.g. the $t_{\frac{1}{2}}$ for fish within a contaminated aquatic system may be quite different from the clearance $t_{\frac{1}{2}}$ measured in the laboratory. Additionally, the reader should note that first-half-lives are not necessarily

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[α] The first-half-life is used here to denote the time to 50% disappearance of a pollutant. Because of changes in reaction mechanisms or kinetics, subsequent half-lives may not be of equal length.

Table 2-5. Reported first-half-life of aminocarb in environmental compartments.

Compartment	$t_{1/2}$ (d)	Reference
Water	3	Murphy et al. (1975b)
	4-7, 11	Sundaram et al. (1976)
	3.5	Minor (1978)
	0.6	Coady (1978)
	0.5-1.5	Elner et al. (1981)
Soil	<1	Murphy et al. (1975a)
	2	Sundaram and Hopewell (1977)
	<1	Minor (1978)
	0.1-0.3	Sundaram (1981)[α]
Conifer Foliage	6	Sundaram et al. (1976)
	3.2-6.9	Sundaram and Hopewell (1977)
	8-11	Barnes (1979)
	<5.5	Sundaram (1981)[α]
Forest Litter	2.6-3.1	Sundaram (1981)[α]
Sediment	3.5	Murphy et al. (1975a)
Invertebrates	<1	Coady (1978)
Plants	<1	Abdel-Wahab et al. (1966)
	<3	Abdel-Wahab and Casida (1967)
Mammals	<2	Krishna and Casida (1966)
Fish	<10[β]	Lamb and Roney (1976)

[α] 1.8D and 1.8F formulations tested.

[β] A component may have a shorter half-life of <0.2 d (see Figure 4-1).

an indicator of the overall dynamics in a system (Roberts et al. 1981). The data base available does not permit this point to be addressed in the case of aminocarb, and firm generalities have yet to be established.

An exception to the reports of relatively short persistence of aminocarb in the environment is seen in its presence in fir needles (35 $\mu g.kg^{-1}$), ground vegetation (13 $\mu g.kg^{-1}$) and soil (11 $\mu g.kg^{-1}$) one year after the area in question had been sprayed (Environmental Monitoring Committee 1979a). Aminocarb was not found in that area after an additional year. Sundaram (1981) reported low levels of aminocarb in balsam fir foliage 21 d after spraying with the 1.8D formulation or the 1.8F formulation (oil or water based). He also reported low levels of aminocarb in forest litter after spraying with either oil-based formulation. He reported no trace in forest soil after 5 d. Carrow et al. (1980) reported 70 $\mu g.kg^{-1}$ aminocarb in forest litter 70 d after spraying, and Parker et al. (1980) reported 2 $\mu g.g^{-1}$ aminocarb and 0.1 $\mu g.g^{-1}$ MAA in blueberry foliage after 60 d. It is possible that conjugates of aminocarb would be detected using direct extraction procedures (see Section 2.6.4).

2.7.1.1 Natural Aquatic Systems

Analyses of natural water bodies to determine the fate of aminocarb in them are few and, in general, much remains to be learned about this subject. Samples of water have been analyzed in conjunction with many field impact studies, but the manner in which the samples were collected was often vague or unknown, making it hard to determine which environmental element was actually sampled.

Following spray applications of 90 g-AI.ha^{-1} (formulated with fuel oil and nonyl phenol), Coady (1978) measured peak concentrations of 24 $\mu g.L^{-1}$ in Newfoundland streams. The peak concentration declined to below detection limits within a day. Similar results were obtained from Quebec streams and lakes. Holmes (1979) monitored two blocks sprayed with aminocarb (formulated with diluent 585 and nonyl phenol) once and twice at 53 g-AI.ha^{-1}. Most aminocarb residues found in streams were 1 $\mu g.L^{-1}$, but he found 3.34 $\mu g.L^{-1}$ in one stream 4.4 h after one spray and 5.71 $\mu g.L^{-1}$ in a lake after two sprays. Holmes (1979) speculated that higher concentrations might be found on the downwind surface of lakes, because aminocarb in oil might stay on the surface and be blown by the wind. Gaboury (1980) surveyed Quebec water bodies for aminocarb residues within operational spray blocks. In lakes and bogs he found concentrations from below the detection limit to 25 $\mu g.L^{-1}$ with a mean of 3 $\mu g.L^{-1}$ in 63 samples. In streams he found residues up to 8.92 $\mu g.L^{-1}$ and a mean of 1.0 $\mu g.L^{-1}$. He also reported 0.133 $\mu g.L^{-1}$ in a lake 5.4 km from a spray block. Elner and Wildish (1981) and Wildish (1980) measured residues in a small pond sprayed with the 1.8D aminocarb formulation at 70 g-AI.ha^{-1}. They used a spray method that delivered a higher-than-normal proportion of the spray to the pond surface (Section 4.4.3). Aminocarb concentration in the pond ranged up to 53 $\mu g.L^{-1}$ 13 h

after spraying and 0.9 $\mu g.L^{-1}$ 12 d later. Three metabolites (FA, AC and MAC) persisted for 24 d. FC was not detected.

Ernst et al. (1981) analyzed water, sediment, and freshwater clams (Anodonta sp.) for aminocarb in two lakes in New Brunswick in 1979. The area was sprayed operationally at 86 $g\text{-}AI.ha^{-1}$ and the larger lake was surrounded by a 400-m buffer zone. They found less aminocarb in the water of the larger lake than in that of the smaller, and suggested that the buffer zone was a useful protective device. They found no aminocarb in sediments or tissues of freshwater clams and unidentified aquatic macrophytes.

Concentrations of aminocarb in natural woodland waters due to aerial spraying rarely exceed 10 $\mu g.L^{-1}$ and even then they are transitory. Unfortunately not all streams are protected by trees, which can filter out over half of the spray reaching the canopy. Also, oil solutions may not mix readily in water, but undergo partitioning to the surface or to lipophilic elements of the milieu. Organisms that live in places where the chemicals concentrate would thus be more exposed. Some high concentrations have been cited, e.g. 81 $\mu g.L^{-1}$ in a Newfoundland pond 36 h after spraying at 70 $g\text{-}AI.ha^{-1}$ (Osborne 1979), but these are possibly artifacts. However, given the broad nature of these studies, there is always the concern that the partitioning of the pesticide could result in local concentrations with deleterious effects on the associated organisms.

2.7.1.2 Model Aquatic Systems

Several mathematical models have been developed as preliminary screens for pollutant behavior in the environment (e.g. Roberts et al. 1981; Neely 1979).

The four-compartment computer model developed by Roberts et al. (1981) (Figure 2-7) generates an algebraic solution that describes the predicted distribution and the degradation and transfer rate constants of the pollutant when a specific system is at steady state and first-order kinetics pertain. As well, pollutant dynamics can be simulated for several scenarios. Both pollutant and system-specific variables are considered in the computations although the model does not attempt to generate absolute values or aspire to simulate natural ecosystems. Here, this model is used to identify some of the critical factors affecting the persistence of aminocarb in aquatic systems and to show the potential range of persistance in different types of water bodies. Some of the limitations of the data base are identified.

Two standardized aquatic systems (Table 2-6), a small, 1 m deep, eutrophic pond and a larger, 15 m deep, oligotrophic lake, are used to compare the relative importance of various processes to the

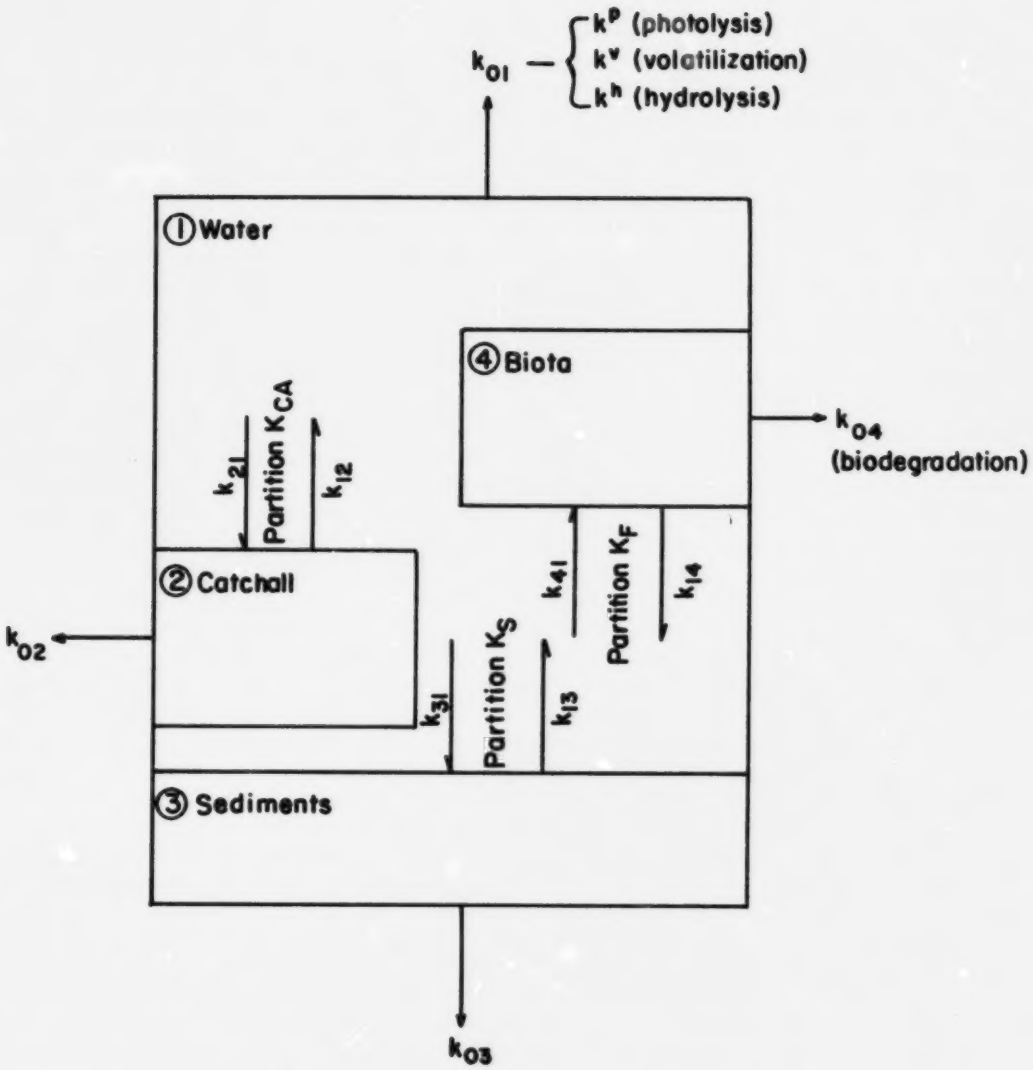

Figure 2-7. Schematic of four-compartment model (Roberts et al. 1981). k_{12}, k_{21}, k_{13}, k_{31}, k_{14}, k_{41} = first-order transfer rate constants, K_{CA}, K_S, K_F = partition coefficients between each compartment and water, k_{01}, k_{02}, k_{03}, k_{04} = first-order removal rate constants.

Table 2-6. Definition of the standard aquatic systems.

	Pond	Lake
Latitude (°N)	45	45
Temperature (°C)	20	20
Water		
Mean depth (m)	1	15
Volume (L)	3.7×10^6	1.0×10^{10}
Suspended solids ($mg.L^{-1}$)	160	16
Non-pollutant light attenuation coefficient	high[α]	low[β]
Sediment		
Weight (g)	7.3×10^7	2.9×10^{10}
Effective depth (cm)	1	1
Organic matter (%)	32	32
Biota		
Number of fish	185	5×10^5
Average weight of each fish (g)	100	100

[α] Light absorption for six polluted water bodies; see Zepp and Cline (1977).

[β] Light absorption for distilled water.

overall fate of aminocarb. The philosophy and limitations behind this approach are fully discussed in Roberts et al. (1981).

The specific input data required to run the computer program for aminocarb include vapor pressure (1.7×10^{-5} mm Hg), melting point (93°C), molecular weight (208.3), solubility (2000 $mg.L^{-1}$), octanol:water partition coefficient (58 at pH 7; 8 at pH 5), first-order hydrolysis rate constant (2.4×10^{-2} d^{-1} at pH 7; 7.6×10^{-3} d^{-1} at pH 5), extinction coefficients for light absorption in the range 290-400 nm and the quantum yield. With the exception of the quantum yield, these parameters have all been determined as previously described. While aminocarb absorbs sunlight only weakly, direct photolysis occurs. Experimentally, photodegradation appears to follow first-order kinetics with a $t_{\frac{1}{2}}$ of 10 d, in a stirred, aerated solution (Mulkey et al. 1978). Sensitization increases the rate of this process under laboratory conditions (Mulkey et al. 1978). The efficiency of the unsensitized reaction is unknown, but the maximum possible influence of direct photolysis on the fate of aminocarb can be examined by setting the quantum yield at 1 in the model. Likewise, the fate of aminocarb, in the absence of photolytic processes can be examined by using a quantum yield of 0. The role of natural sensitizers in the environment is unknown and cannot be predicted using the current data base.

Microbial processes are likely to contribute to the degradation of aminocarb, but the rates of such processes in natural systems are unpredictable. In order to determine the magnitude of such processes required in sediment or suspended solids, if they are to significantly contribute to the overall fate of aminocarb, the model was set to predict the rate constants which would result in total microbial processes accounting for 10% of the total degradation. In all runs of the model, it was arbitrarily assumed that upon absorption, 100% of the aminocarb is degraded by fish.

The patterns predicted at equilibrium (the fixed solutions) for both the pond and lake under neutral and acidic conditions are detailed in Table 2-7. These predictions indicate that even direct photolysis could conceivably compete with hydrolysis as the main removal process, if this process was efficient (quantum yield ~ 1). In the absence of photolysis and at neutral pH, a sediment microbial degradation rate constant of about 1×10^{-2} d^{-1} in the pond or about 7×10^{-2} d^{-1} in the lake, is necessary for this process to compete with hydrolysis (to contribute 5% to total removal of aminocarb). When photolysis is maximized, these rate constants must be increased to about 3 d^{-1} and 6 d^{-1} respectively. Volatilization does not contribute significantly to aminocarb fate in any of the situations modelled. However, the model assumes aquatic systems to be homogeneous and aminocarb formulated in oil might form a surface slick and be more susceptible to volatilization. The size of the sediment pool (which is relatively bigger in the pond than in the lake) does not have a dramatic influence on the persistence of aminocarb which, because of its high

Table 2-7. Computer model predicted distribution and degradation of aminocarb in the standard pond and lake.

	pH 7				pH 5	
	Maximum Photolysis		Minimum Photolysis		Maximum Photolysis	Minimum Photolysis
	Pond	Lake	Pond	Lake	Pond	Pond
Retentive capacity of system (d)[α]	0.14	0.05	43.3	38.2	0.13	119.8
First order $t_{\frac{1}{2}}$ (d)	0.18	0.03	29.3	26.5	0.09	83.04
Percent of total load sequesteral in:						
water	85.5	98.1	88.5	98.1	98.2	98.2
suspended-solids	0.3	~ 0	0.3	~ 0	~ 0	~ 0
sediment	11.2	1.8	11.2	1.8	1.7	1.7
fish	~ 0	~ 0	~ 0	~ 0	~ 0	~ 0
Percent of total removal due to:						
volatilization	~ 0	~ 0	0.1	~ 0	~ 0	0.2
photolysis	90.2	90.4	0	0	90.4	0
hydrolysis	0.3	0.1	89.9	89.9	0.1	89.4
microbial breakdown[β]	10	10	10	10	10	10
biodegradation in fish	~ 0	~ 0	0.5	0.5	~ 0	0.8

[α] The retentive capacity is the inverse of the specific rate of removal of pollutant from the system at any time.

[β] Includes 5% breakdown in sediment and 5% breakdown in suspended solids.

water solubility, is mostly retained in the water compartment. As mentioned, hydrolysis is known to be more efficient at an alkaline pH. However, the octanol-water partition coefficient also varies with pH so that, at alkaline pH, more aminocarb is sequestered in the water compartment and is potentially available for degradation by photolysis and hydrolysis. The model predicts (Table 2-7) that, if photolysis is an efficient process, the two effects could essentially cancel one another resulting in a similar retentive capacity at pH 5 and pH 7. However, if photolysis is inefficient, aminocarb is predicted to be at least twice as persistent at pH 5 as at pH 7. Of course, microbial processes may play a very different role from that predicted by the model. In turbid water, where photolysis would be slow because of light attenuation, the microbial density could be relatively high. The measured half-lives of aminocarb in water of 0.5-11 d (Table 2-5) are in the range predicted by the computer model (0.05-120 d).

2.7.2 NONYL PHENOL

Sundaram et al. (1980) found the following half-lives for nonyl phenol after a forest spray: (a) 3 h in stream or pond waters (detection limit 1 $\mu g.L^{-1}$) with none detected after five days; (b) 3 h in white spruce foliage (detection limit 0.20 $mg.L^{-1}$) with none detected after 30 days. Nonyl phenol residues above the detection limit of 0.05 $mg.kg^{-1}$ were found only in one sediment sample collected from the stream in question, and it was not detected in any soil (detection limit 0.10 $mg.kg^{-1}$) or fish (detection limit 1 $mg.kg^{-1}$) sample taken up to 10 d after the spray. Brun and MacDonald (1981) also developed a method of analysis for nonyl phenol by HPLC with a UV (278 nm) detector; the minimum detectable levels are 1 $\mu g.kg^{-1}$ in water and 0.3 $mg.kg^{-1}$ in sediment.

Holmes and Kingsbury (1980) studied the environmental dynamics of nonyl phenol in a stream sprayed experimentally in Ontario. The spray mixture consisted of 30.28 L nonyl phenol, 62.46 L 585 diluent oil, and 1.89 L automate "B" dye. It was emitted at a rate of 1.46 $L.ha^{-1}$ giving a rate of 467 mL nonyl phenol.ha^{-1}. In flowing water, at one site, residues were 9.1, 4.3 and 2.3 $\mu g.L^{-1}$ 1, 2, and 4 h after spraying. Traces (< 2.0 $\mu g.L^{-1}$) were found in some samples up to 5 d after spraying. At another site, only traces were found in some samples. In "near-stagnant" water, 1100 $\mu g.L^{-1}$ were found in the 4 h postspray sample. This extremely high concentration diminished to 110, 12, and 2.4 $\mu g.L^{-1}$ by the 6th, 24th, and 48th postspray hours respectively, and traces were found in some samples up to 5 d after spraying. This difference between flowing and standing water has typically been reported following forest spraying (Lockhart et al. 1973). In stream sediments only one sample contained a measurable residue (0.05 $mg.kg^{-1}$). Ernst et al. (1981) found nonyl phenol in a small lake 48 h after operational spraying at 86 $g.ha^{-1}$. The model of Eidt and Sundaram (1975) predicts concentrations of 10-20 μg nonyl phenol.L^{-1} after operational sprays at 70-87 $g.ha^{-1}$ in a well mixed woodland stream.

On the basis of the limited data available, nonyl phenol appears not to be persistent in any environmental compartment examined to date. However, studies have examined only the persistence of the parent compound and have not considered any chemical reactions or the nature and persistence of their products. Also, there is the concern that partitioning of nonyl phenol could result in high local concentrations.

3.0 EXPOSURE

It is generally accepted that the protection of timber stands from insect damage, by means of aerial insecticide spraying, could pose a risk to the health of organisms in the area. The level of risk is defined in part by the actual exposure encountered by an organism. Pesticides are released from the aircraft as an aerosol. A cloud is formed which conforms to the aircraft wake and which may be dispersed somewhat by atmospheric turbulance as it descends (Wickens 1980; Bilanin et al. 1978). Atmospheric flow patterns, temperature, spray droplet size and the topography of the area all affect the spray deposition pattern and hence the exposure encountered by various organisms (NRCC 1975).

The exposure is defined, in part, by:

1. The magnitude and duration of the airborne concentration of atomized droplets in and above the target canopy.
2. The size spectrum of the droplets.
3. The potential drift of a significant fraction of these droplets to non-target areas downwind from the application zone.
4. The direct deposition of pesticide onto areas not protected by the forest canopy, such as forest meadows, exposed ridges, streams or other small water bodies.
5. The occurrence of human errors which can lead to oversprays.

The range of deposits and the possible scenarios associated with a given spray program make it hard to interpret the observed effects of the program in terms of the amount of spray reaching potential receptor organisms. Similarly, it is hard to predict the exposure threat to organisms inhabiting a particular environmental compartment from the properties of the chemical and environmental conditions.

Scenarios have been developed from which theoretical "worst-case" human exposure can be predicted for the inhalation, dermal and ingestion routes (e.g. NRCC 1979; Houghton 1978; Franklin et al. 1981). Houghton (1978) suggested that the "worst-case" should anticipate the maximum exposure which could occur but should not subject the pesticide to an "unfair assessment". In practice, our data base is so limited that any such scenarios involve multiple assumptions which may result in a distorted assessment of risk. What is "an unfairly stringent assessment" is open to debate and it is extremely important to understand the implications of the assumptions and limitations of models.

Some of the grossest assumptions used in these scenarios are associated with the prediction of the airborne insecticide concentrations encountered by a receptor. In an attempt to refine our predictive capabilities, a computer model has been developed to predict airborne insecticide concentrations for the forest spray program in New Brunswick (Crabbe and Reid 1980).

3.1 A COMPUTER MODEL FOR THE DRIFT AND DEPOSITION OF AN AERIAL AMINOCARB SPRAY ONTO A FOREST

The computer model simulates the drift and dry deposition of aminocarb after aerial application onto a forest. Initial spray cloud descent in the vortex wake, airborne drift, spray evaporation, upper foliage droplet collection and downward transfer of droplets by sedimentation and turbulence into the lower canopy are modelled. Mathematical details are given in Reid and Crabbe (1980) and Crabbe and Reid (1980). Details of the spray scenario adopted in the present model and model input are presented in Appendix III.

Briefly, the model computes the concentration of airborne droplets downwind of an aerial spray, in light winds (50 $cm.s^{-1}$ at tree height), over a coniferous forest. The spray droplets are confined within the aircraft vortex wake as it descends to the forest, at which point the vortex pair separates laterally and gives rise to a homogeneous aerosol cloud 410 m wide which extends vertically from mid-canopy to just above the trees. The reader will recognize 410 m as the value adopted by New Brunswick spray operations for the swath width, or interval, of a three-aircraft team of TBM spray planes. The aminocarb application rate used in the model is the New Brunswick operational value of 70 $g\text{-}AI.ha^{-1}$ for a model source strength of 2.9 g per metre of flight line.

Although the model addresses the case of a single operational swath, the concentration pattern from a multi-swath operation is the sum of a sequence of statistically identical single-swath patterns extending upwind at 410 m intervals. However, the predicted peak concentration is not altered in this way. Consequently, only one swath is analyzed.

Partial model validation is contained in Crabbe and Reid (1980) where the predicted percent active ingredient still airborne at 7.5 and 24 km downwind of an aerial forest spray agreed quite well with field data (Crabbe et al. 1980b). The model performance is further discussed in Appendix III.

3.2 PREDICTION OF EXPOSURE OF HUMAN BYSTANDERS TO AMINOCARB

Here, we estimate the potential bystander exposure to aminocarb using both standard "worst-case" scenarios and computer predicted concentrations. The standard scenarios used here have been developed by Agriculture Canada and/or Health and Welfare Canada (e.g. Houghton 1978; Franklin et al. 1981) except where noted. Data from the computer model (Appendix III) have been used as indicated.

3.2.1 DERMAL EXPOSURE

If we define the aminocarb application rate as X $g.ha^{-1}$ then, under normal conditions, the maximum quantity deposited per m^2 would be:

$$\frac{X}{10,000} = 1 \times 10^{-4} \times X \text{ g} = 0.1 \times X \text{ mg}$$

A certain proportion of this quantity will usually be intercepted by target foliage and some may drift away. However, in the worst case (e.g. an organism in a forest clearing), 100% of the depositing spray could land on the skin of the organism.

In the case of humans, most scenarios assume a 70 kg man with 15% of a total 2 m^2 body surface exposed, although it is not safe to assume that areas covered by clothing are completely protected (Federal Working Group on Pest Management 1974). In this case (15% of 2 m^2 exposed) the maximum potential dermal contact would be:

$$2 \times 0.15 \times 0.1 \times X \times \frac{1}{70} = 4.29 \times 10^{-4} \times X \text{ mg.kg-BW}^{-1}$$

The predictions of the computer model can also be used to estimate dermal exposure. The exposed areas of a bystander (head, neck, hands, forearms) are represented as flat plates normal to the droplet trajectories. Details are confined to Appendix III, where it is shown that the model-estimated dermal exposure of an unsheltered bystander at a spray line is $9.54 \times 10^{-5} \times X$ $mg.kg\text{-}BW^{-1}$, in a wind of 50 $cm.s^{-1}$.

The present computer model does not calculate subcanopy exposure. However, Appendix III shows that the subcanopy time-integrated concentration at the spray line may be expected to be about 6% of that for an unsheltered area, based on the field data of Crabbe et al. (1980a). Thus, the potential dermal exposure for a bystander in the woods, sheltered by the canopy, is estimated to be about $6 \times 10^{-6} \times X$ $mg.kg\text{-}BW^{-1}$, inasmuch as the exposure is approximately proportional to the time-integrated atmospheric concentration.

The computer-estimated exposure is lower than the exposure estimated using the more conventional scenarios, principally because the depositing material is wind-blown and the computer model reveals that droplets smaller than about 75 µm, which contain about 25% of the original spray mass, will flow around rather than impact on the bystander. The other scenarios assume that all droplets have 100% impact efficiency irrespective of their diameter. Because the depositing mechanism is mainly inertial impaction, model computations reveal that a doubling of the wind speed raises the predicted dermal exposure from $9.54 \times 10^{-5} \times X$ to $2.63 \times 10^{-4} \times X$ $mg.kg\text{-}BW^{-1}$.

At the current application rate for aminocarb, 70 $g\text{-}AI.ha^{-1}$, the potential worst-case dermal exposure for a 70 kg human bystander is thus estimated to be 6.7×10^{-3} $mg.kg\text{-}BW^{-1}$ in light winds. If the

bystander is protected by the forest canopy, this figure is reduced to about 0.5 $\mu g.kg\text{-}BW^{-1}$. Doubling the treetop wind speed to 100 $cm.s^{-1}$ raises these estimates to 1.84×10^{-2} $mg.kg\text{-}BW^{-1}$ and 1 $\mu g.kg\text{-}BW^{-1}$ respectively.

3.2.2 INHALATION EXPOSURE

Inhalation exposure may result from the respirable droplet component of the spray cloud and/or from vaporization of aminocarb during and after deposition (Houghton 1978). The droplet size spectrum of the spray influences its movement down the respiratory system. Particles smaller than ~ 5 µm in diameter can be deeply inspired to the alveolar region and subsequently absorbed to reach the circulatory system (Task Group on Lung Dynamics 1966; Franklin et al. 1981). Particles >5 and <50 µm in diameter may lodge in the nasopharyngeal compartment or elsewhere high in the respiratory system (Houghton 1978). These particles are soon swallowed (Task Group on Lung Dynamics 1966) and have been considered as oral exposure. Particles >50 µm in diameter fall too rapidly to be inhaled (Houghton 1978) and can be ignored. Operational spray conditions in Eastern Canada generate the droplet-size distribution shown in Figure 3-1 (Crabbe 1982). A very small percentage of the aminocarb mass resides in droplets <5 µm in diameter; 0.5% may be used for a "worst-case" analysis.

In the "worst-case" scenario, all the aminocarb released from an aircraft over a given area reaches an organism occupying that area. A human bystander can be assumed to occupy a "contained" space 2 m^2 x 3 m (Franklin et al. 1981) so that the volume surrounding him is 6000 L. At an application rate of X $g.ha^{-1}$, the concentration of aminocarb in this space is:

$$\frac{0.1 \times X \times 2}{6000} mg.L^{-1} = 0.2 \times X \text{ mg.6000 } L^{-1}$$

The concentration available for deep inspiration is:

$$\frac{0.2 \times X \times 0.005}{6000} = 0.001 \times X \text{ mg.6000 L}$$

Assuming a respiration rate of 29 $L.min^{-1}$ (Franklin et al. 1981), the inhalation exposure becomes:

$$29 \times \frac{0.001 \times X}{6000} \times 60 = 2.9 \times 10^{-4} \times X \; mg.h^{-1}$$

Correcting for body weight:

$$\frac{2.9 \times 10^{-4} \times X}{70} = 4.14 \times 10^{-6} \times X \; mg.kg\text{-}BW^{-1}.h^{-1}$$

Of course, this is undoubtedly an overestimate. The concentration of aminocarb at the deposition site is actually predicted by the computer model to decrease through several orders of magnitude

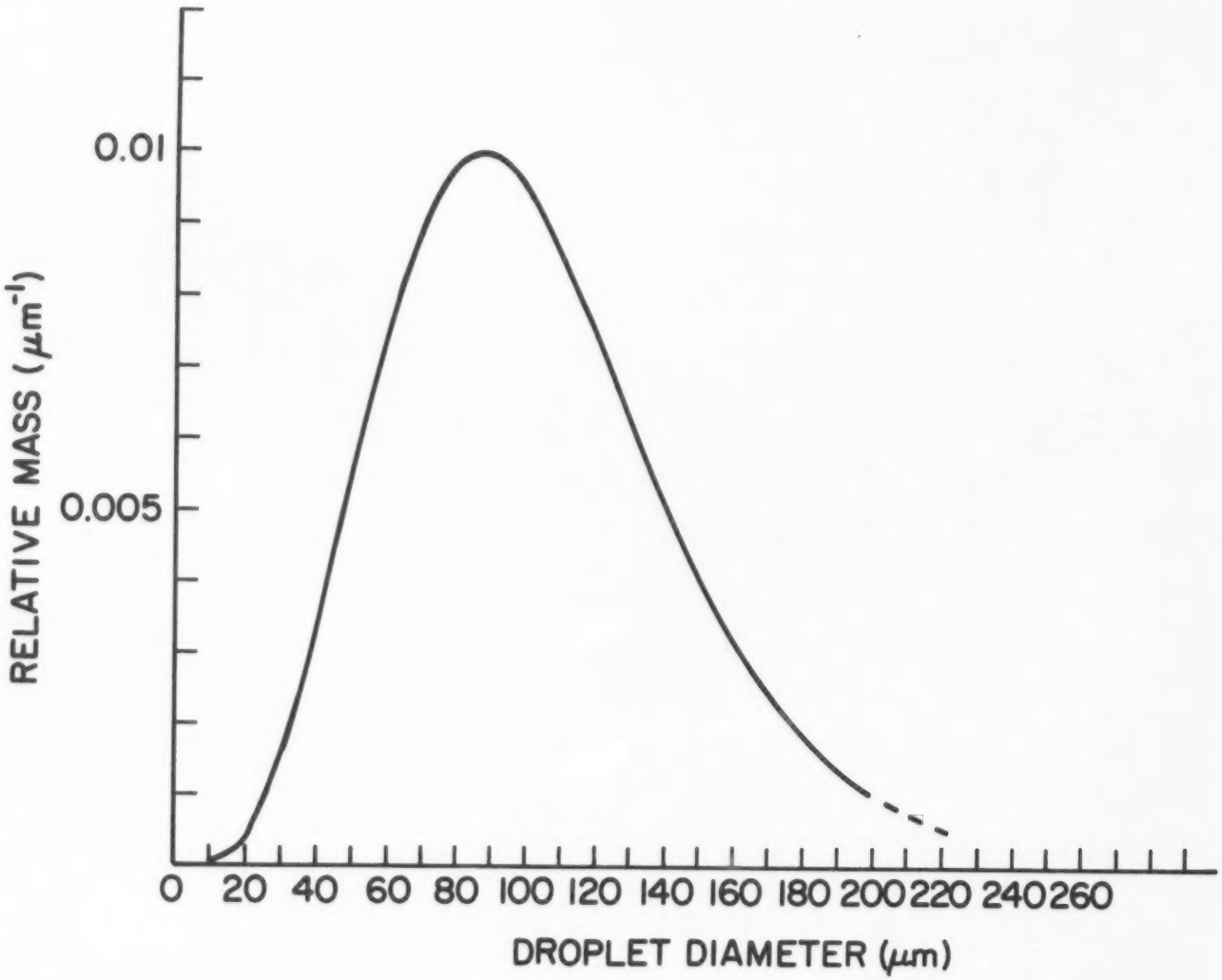

Figure 3-1. Initial aminocarb spray mass distribution (Crabbe 1982).

within minutes (Figure 3-2). Thus, as shown in Appendix III, an unsheltered bystander at the spray line in light winds, would inhale only a total dose of $1.33 \times 10^{-8} \times X$ mg.kg-BW^{-1} when the highly transient nature of the concentration field is taken into account. As was noted earlier however, subcanopy inhalation exposure would likely be only 6% of this figure, $7.8 \times 10^{-10} \times X$ mg.kg-BW^{-1}. This total dose would be received in about 3.5 minutes at the spray line.

At an application rate of 70 g-AI.ha^{-1}, in light winds, the computer predicted human bystander inhalation exposure would thus be estimated as 9.3×10^{-7} mg.kg-BW^{-1} or about 5.5×10^{-8} mg.kg-BW^{-1} for a bystander sheltered by the forest canopy.

Doubling the model treetop wind speed to 100 cm.s^{-1} reduces the predicted time-integrated droplet concentration at the spray line, and hence the inhalation exposure, by about 30%.

3.2.2.1 Estimation of Vapor Exposure

The theoretical aerial concentration for pure aminocarb can be predicted from its vapor pressure (p) and the gas law:

$$pV = nRT$$

where p is in 2.237×10^{-8} atmospheres[α] (Addison 1981b), V is the volume occupied (cm^3), n is the number of moles of aminocarb in V, and R is the gas constant (82.06 cm^3.atm.deg^{-1}.mol^{-1}) and T is the temperature in °K. The concentration at 10°C can be estimated:

$$\frac{n}{V} = \frac{P}{RT} \text{ mol.cm}^{-3}$$

$$= \frac{2.237 \times 10^{-8}}{82.06 \times 283} \text{ mol.cm}^{-3}$$

$$= 1.94 \times 10^{-7} \text{ mg.L}^{-1}$$

The particle size spectrum for this situation is not known. Assuming that all this material is available for deep inspiration (a likely overestimate), and a respiration rate of 29 L.min^{-1} (Franklin et al. 1981), the vapor inhalation exposure for a 70 kg man becomes:

$$\frac{29 \times 1.94 \times 10^{-7} \times 60}{70} = 4.82 \times 10^{-6} \text{ mg.kg-BW}^{-1}.\text{h}^{-1}$$

[α] 1 atmosphere = 101.325 kPa.

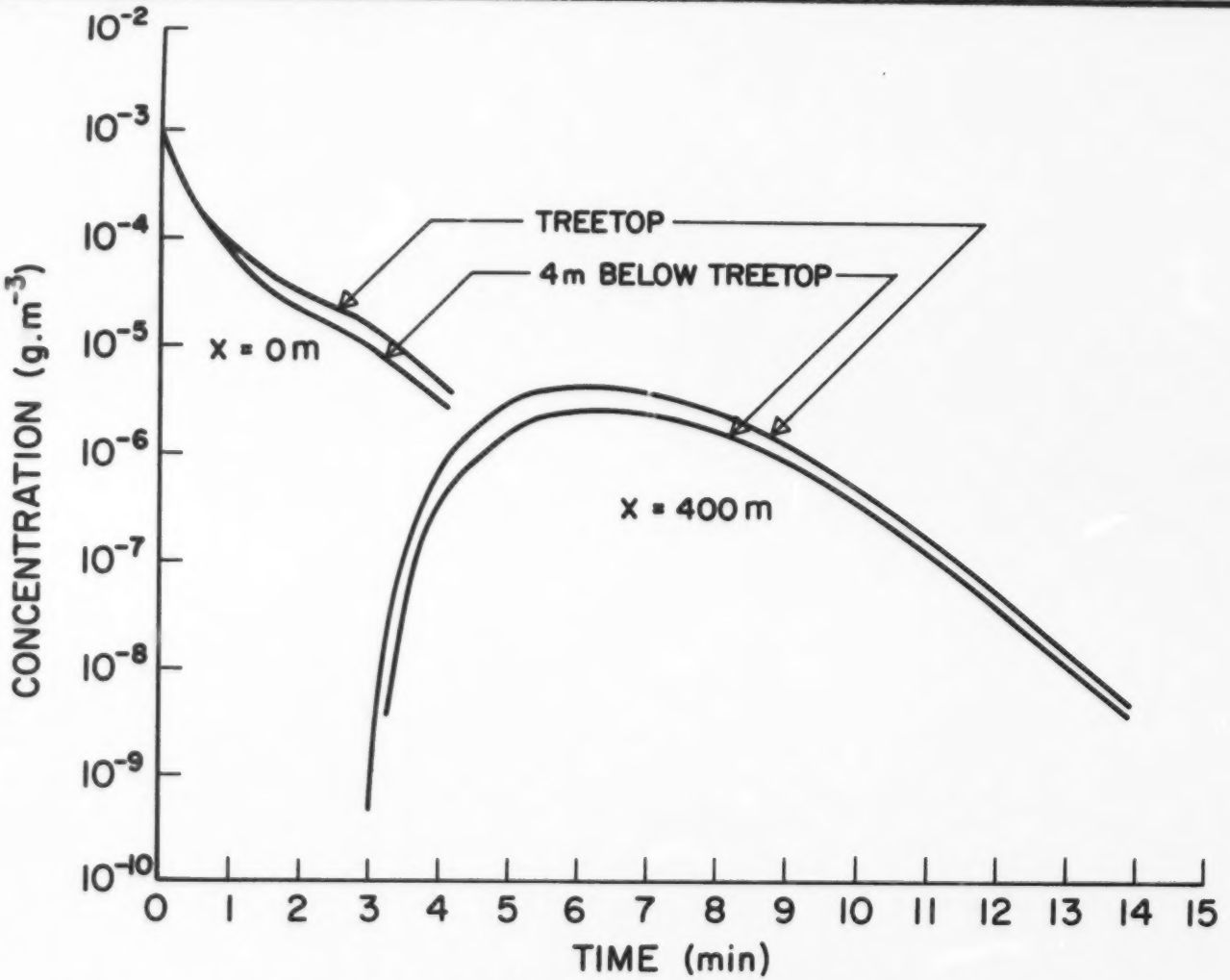

Figure 3-2. Model-predicted atmospheric concentration of aminocarb from an aerial spray swath of 2.87 g per metre of flight line (70 g-AI.ha^{-1}) in light winds (Crabbe 1982).

x is the distance from the spray line.

This exposure would apply to aminocarb sprayed at any rate sufficient to allow vapor saturation in the atmosphere at and below 3 m. The minimum theoretical application rate for such potential saturation would be 0.2 $mg.ha^{-1}$. At lower temperatures (such as the 5°C of the computer scenario) the vapor exposure would, of course, be somewhat lower.

3.2.3 ORAL EXPOSURE

Oral exposure to bystanders arises from the inhalation of the relatively large droplets (between approximately 5 and 50 μm) which are moved from the trachea to the hypopharynx and are subsequently swallowed (Task Group on Lung Dynamics 1966; Franklin et al. 1981). Obviously, application workers may be subjected to additional oral exposure, especially if hygiene practices are poor. From the distribution in Figure 3-1 it can be shown that at the spray line, 7% of the spray of aminocarb resides in droplets smaller than 50 μm in diameter.

Thus, for a human bystander, the potential "worst-case" oral exposure is 7%/0.5% or 14 times the potential inhalation exposure, i.e. $5.8 \times 10^{-5} \times X$ $mg.kg\text{-}BW^{-1}.h^{-1}$.

Using the concentrations predicted by the computer model (see Appendix III), the estimated oral exposure for an unsheltered bystander at the spray line in light 50 $cm.s^{-1}$ winds, would be about $1.9 \times 10^{-7} \times X$ $mg.kg\text{-}BW^{-1}$ when the highly transient nature of the concentration field is taken into account. As before, a canopy shelter would likely lower this figure to about $1.1 \times 10^{-8} \times X$ $mg.kg\text{-}BW^{-1}$.

At an application rate of 70 $g\text{-}AI.ha^{-1}$, the computer-predicted oral exposure is thus estimated to be 1.3×10^{-5} $mg.kg\text{-}BW^{-1}$ or 8×10^{-7} $mg.kg\text{-}BW^{-1}$ if the bystander is protected by the forest canopy.

As before, a doubling of the modelled wind speed reduces these exposures by about 30% at the spray line.

3.3 SUMMARY OF ESTIMATED TOTAL HUMAN BYSTANDER EXPOSURE

For aminocarb sprayed at a rate of X $g\text{-}AI.ha^{-1}$, the estimated total "worst-case" exposure in 1 hour would be:

Dermal -	$- 4.29 \times 10^{-4} \times X$ $mg.kg\text{-}BW^{-1}$
Inhalation - particulate	$- 4.14 \times 10^{-6} \times X$ $mg.kg\text{-}BW^{-1}$
vapor exposure	$- 4.8 \times 10^{-6}$ $mg.kg\text{-}BW^{-1}$
Oral -	$- 5.8 \times 10^{-5} \times X$ $mg.kg\text{-}BW^{-1}$
Total (less vapor exposure)	$- 5.0 \times 10^{-4} \times X$ $mg.kg\text{-}BW^{-1}$

At the current application rate, 70 $g\text{-}AI.ha^{-1}$, the total exposure is estimated as 0.035 $mg.kg\text{-}BW^{-1}$.

Using the predictions of the computer model (Appendix III) the total estimated exposure, in light winds, for an unsheltered bystander at the spray line is:

Dermal -	$- 9.54 \times 10^{-5} \times X$ mg.kg-BW^{-1}
Inhalation - particulate	$- 1.3 \times 10^{-8} \times X$ mg.kg-BW^{-1}
Oral -	$- 1.9 \times 10^{-7} \times X$ mg.kg-BW^{-1}
Total -	$- 9.56 \times 10^{-5} \times X$ mg.kg-BW^{-1}

At the current application rate of 70 g-AI.ha^{-1}, the total exposure (less vapor) for an unsheltered bystander is estimated by the computer model to be 6.7×10^{-3} mg.kg-BW^{-1}. A doubling of the model wind speed from 50 to 100 cm.s^{-1} at treetop, raises this estimate to 1.9×10^{-2} mg.kg-BW^{-1} at the spray line.

3.4 EXPOSURE RISK TO ORGANISMS DOWNWIND FROM THE SPRAY LINE

The computer model has been used to estimate exposure at 400 m and 800 m downwind from the spray line. The method follows that of Appendix III. In computing the dermal and oral exposure, account was taken of the progressive change in airborne droplet size distribution with downwind distance.

At 400 m the model predicted exposures (mg.kg-BW^{-1}) are:

	Treetop wind speed (cm.s^{-1}) 50	100
Dermal -	$- 4.3 \times 10^{-8} \times X$	$3.9 \times 10^{-6} \times X$
Inhalation - particulate	$- 1.1 \times 10^{-9} \times X$	$1.0 \times 10^{-9} \times X$
Oral -	$- 1.9 \times 10^{-7} \times X$	$9.6 \times 10^{-8} \times X$
Total -	$- 2.3 \times 10^{-7} \times X$	$4.0 \times 10^{-6} \times X$

At 800 m the model predicted exposures (mg.kg-BW^{-1}) are:

	Treetop wind speed (cm.s^{-1}) 50	100
Dermal -	$- \sim 0$	$1.0 \times 10^{-6} \times X$
Inhalation - particulate	$- 6.4 \times 10^{-10} \times X$	$4.6 \times 10^{-10} \times X$
Oral -	$- 1.2 \times 10^{-7} \times X$	$5.4 \times 10^{-8} \times X$
Total -	$- 1.2 \times 10^{-7} \times X$	$1.0 \times 10^{-6} \times X$

Downwind from the spray line, the dermal exposure is dominant at the higher wind speed while, at the lower wind speed, almost all the exposure is via the oral route.

Because of the increased percentage of smaller droplets with better mixing potential, the subcanopy exposures at 400 m and 800 m downwind of the spray line are expected to be about 12% and 40% respectively of those at tree height, based on the field data of Picot et al. (1980). This contrasts with the situation at the spray line, where the subcanopy exposure was estimated to be only about 6% of that at tree height.

At current application rates (70 g-AI.ha^{-1}), the computer-estimated total exposure for an exposed bystander at 400 m and 800 m downwind of the spray line is 1.6×10^{-5} and 8.4×10^{-6} mg.kg-BW^{-1} respectively at a wind speed of 50 cm.s^{-1} and 2.8×10^{-4} and 7.4×10^{-5} mg.kg-BW^{-1} respectively at the higher wind speed of 100 cm.s^{-1}. This exposure would be received in less than 30 min in both cases.

The possibility of long-range spray drift of forest pesticides has been raised. For example, Pearce et al. (1980) found that rain 85 km from the nearest spray block contained 0.16 µg.L^{-1} of fenitrothion, Pearce and Brun (1980) found 0.3 µg.L^{-1} of aminocarb in rain 45 km from the nearest spray block and Gaboury (1979) reported 1.2 µg.L^{-1} of aminocarb in lakes and ponds located as far as 5 km from spray blocks. Crabbe et al. (1980b) have measured windborne droplet drift 22 km from an aerial spray.

3.5 ABSORBED DOSAGE

For the exposure routes described above, the main barrier to pesticide absorption into the bloodstream will be the skin, lungs and gastrointestinal tract. Absorption across these barriers is discussed by Franklin et al. (1981). Except for local contact effects, pesticides exert their toxic effects after being absorbed into the bloodstream. For this reason it is sometimes useful to predict the absorbed dosage: total exposure x % absorbed.

The extent of absorption across skin on different areas of the body varies up to 42-fold (Federal Working Group on Pest Management 1974). The extent of absorption depends on the thickness of the outer lipid layer (sebum) of the skin. Follicle-rich areas allow the greatest penetration of chemical (Franklin et al. 1981). The extent to which aminocarb is absorbed through the skin is not known. Alveolar absorption is thought to be ~ 100% (Lippman et al. 1980). Absorption across the gastrointestinal tract is complex and it is usually reasonable to presume 100% absorption (Franklin et al. 1981).

A more specific estimate of absorbed dosage may be made by measuring levels of a pesticide and/or its metabolites in blood or urine or, in some cases, some toxic response may be measured e.g. inhibition of an enzyme (Section 3.7).

3.6 MARGIN OF SAFETY

The toxicology of aminocarb is discussed in considerable detail in chapters 4 and 5. No-observed-effect levels (NOELs) for laboratory mammals (2-5 $mg.kg\text{-}BW^{-1}.d^{-1}$) could be used to estimate margins of safety for humans for application of aminocarb at a given rate. It is important to remember that the response of man may be very different from the response of a laboratory mammal. Also, there may be a variation in sensitivity from one person to another.

3.7 CHEMICAL DETECTION OF HUMAN EXPOSURE

Only scant information is available about the detection of asymptomatic human exposure. In man as in other mammals, it is probable that signs and symptoms due to cholinesterase inhibition (Section 5.2) do not become recognizable until enzyme activities in most tissues are reduced by at least 50 percent. Certainly in poisonings due to organophosphorus insecticides, cholinesterase inhibition appears before and lasts much longer than the clinical illness (Gosselin et al. 1976). The nonspecific plasma esterases (pseudocholinesterase and aliesterases) appear to be more sensitive than acetylcholinesterase to inhibition by most organophosphorus and carbamate insecticides, including aminocarb (Baron et al. 1964). Therefore assays for these enzymes should in principle be a nearly ideal way to detect subclinical human exposures. In practice such assays are far from satisfactory indicators, particularly at low-level exposures. As noted above, the rapid, spontaneous reversal of inhibition is one major problem. The enzyme may thus recover its activity between the time the specimen is taken and the time it is analyzed. Furthermore, each of the common assay procedures (manometric, titrimetric, etc.) is subject to many variables which have not been widely standardized. Finally, as a way of detecting aminocarb exposure, all cholinesterase measurements lack specificity. Many drugs, pesticides and other environmental chemicals are also capable of inhibiting esterases *in vivo*.

The chemical analysis of blood and urine for aminocarb or its metabolites is an alternative strategy. For example, the analysis of urine for p-nitrophenol is a useful method of detecting human exposure to parathion, chlorthion and EPN (Roan et al. 1969). No data on aminocarb metabolite levels in human urine were located in the open literature. One report (Everett 1965) describes a colorimetric analysis of human urine to detect aminocarb exposure in the personnel of a plant manufacturing and packaging aminocarb. This method is detailed in Chapter 2. Twelve individuals with potential occupational exposure to aminocarb were tested; most of their spot urine samples yielded values of $< 3\ mg.L^{-1}$ but occasional readings rose to $12\ mg.L^{-1}$, and in two specimens, 72 and $82\ mg.L^{-1}$ were observed. The urines of unexposed persons had values equivalent to $0.2\text{-}2.0\ mg.L^{-1}$.

This procedure is too time-consuming and cumbersome for mass surveys, and it may be too insensitive to detect the low levels involved in nonoccupational exposures.

Further work is highly recommended to develop a simple method of detecting aminocarb metabolites in human urine. The method could then be employed to screen pesticide applicators and workers in plants manufacturing and packaging aminocarb. Ideally, rates of urinary excretion of the metabolites should be computed from the assay data, but it is notoriously difficult to obtain timed urine specimens, such as 24-h collections, even in a controlled hospital environment. Spot urine samples, however, are usually easy to collect. Because the urinary concentration of most solutes varies inversely as the rate of water excretion, it is useful to normalize data on solute concentration in spot urine specimens by adjusting for high and low rates of urine flow. The urinary concentration of endogenous creatinine has sometimes been used for this purpose on the assumption that the creatinine excretion rate is constant and independent of urine flow (Peters and Van Slyke 1946). The assumption is only approximately true, but among healthy persons creatinine is excreted at less variable rates than other common urinary solutes. The rate, however, does depend on body size, notably muscle mass (Peters and Van Slyke 1946). The ratio of the amount of aminocarb metabolite(s) found in a spot urine specimen to the amount of creatinine in the same specimen should be a better index of exposure than the metabolite concentration itself. If the denominator were adjusted according to the size of the subject, an even better index would result. In principle, data on urinary concentration could also be normalized by reference to urine specific gravity, but creatinine concentration is probably a more valid reference.

The significance and utility of data generated in a mass survey like that proposed above cannot be prejudged. Adjusted urinary concentrations of aminocarb metabolite(s) would have to be compared with the medical histories of the subjects before any conclusions could be reached about what exposure levels are hazardous. In Everett's (1965) limited series, unadjusted urinary concentrations of 12 mg (and less) 4-dimethylamino-3-methylphenol per L urine were measured in persons with no symptoms, whereas 72 and 84 $mg.L^{-1}$ were observed in "two reported toxicity cases." If the analytic method can be improved, the potential for developing important information in a large-scale project is judged to be high.

3.8 WILDLIFE EXPOSURE

It is much more complicated to estimate wildlife exposure than human exposure. Behavioral patterns are more varied and greatly influence exposure (Section 4.1).

Models for exposure have not been developed for most species and while aerosol deposition, for example, is known to vary even in

animals of nearly identical size (McMahon et al. 1977), few values are available in the literature. The collection efficiency for droplets depends sensitively on the droplet-size spectrum, the size and geometry as well as the surface characteristics of the receptor and the wind speed (Section 3.0).

Despite these restrictions, exposure has been estimated where possible, using the predictions of the computer model and the types of scenarios discussed above. Details are in the relevant sections of Chapter 4.

4.0 ENVIRONMENTAL TOXICOLOGY

4.1 TERRESTRIAL ECOSYSTEMS

Aerial application of aminocarb, or any insecticide, produces immediate short-term contamination of the forest ecosystem. How the ecosystem responds depends on its sensitivity to the specific contamination. This is determined by two factors: the toxicity of the insecticide to various organisms and the opportunity for exposure of organisms to the chemical and its metabolites. In assessing the sensitivity of an ecosystem to pesticide contamination (or the hazard posed by pesticide contamination) both toxicity and opportunity for exposure, must be considered. Data on toxicity of a pesticide to a variety of standard test organisms (fish, birds, small animals) are routinely collected as part of federal requirements for registration.

The toxicity of a chemical to an organism is a reliable measure of relative susceptibility, but in a natural ecosystem opportunity for exposure is at least as significant in defining impact. Exposure is a complex process, influenced by a variety of natural processes which are not as completely understood as toxicity. While toxicity is relatively static, exposure varies greatly among species, plant communities and sites. Features of behavior, such as habitat selection and seasonal and diurnal patterns of feeding or foraging, are major determinants of exposure. For each compartment within the forest ecosystem, i.e. upper canopy, lower canopy, shrub layer, soil surface, etc., there are certain faunal species which are most threatened by aerial application of insecticides, because of their susceptibility or vulnerability. Surveillance of these "indicator species" is useful in determining at what rates of pesticide application ecological effects first become evident. In the spruce-fir ecosystem, such indicators may include representative species of predators including predaceous birds, arthropods, parasitic wasps and flies, and decomposers. Major disruptions in the population dynamics of these organisms might result in long term changes in ecosystem processes, and are, therefore indicators of a need for more detailed ecological study.

Exposure is also influenced by the duration of persistence of the pesticide (or its adjuvants and metabolites) in various compartments of the ecosystem.

Toxicity resulting from pesticide contamination includes both direct and indirect toxic effects (Varty 1980). Direct effects are manifested as acute effects (e.g. spruce budworm killed by aminocarb) or chronic effects, which may appear as suppressed growth, reproductive anomalies, slow response to predators, etc. The latter have been postulated (e.g. Varty 1980), but not demonstrated in the field for carbamates. Indirect effects are commonly manifested in three ways: bioaccumulation and biomagnification, reduced food supply of non-target

organisms, and disruption of natural biocontrol processes (Varty 1980). Organochlorine insecticides characteristically result in bioaccumulation and biomagnification in the food chain. Because of their relatively short persistence and low octanol:water partition coefficient, organophosphorus and carbamate insecticides generally do not bioaccumulate or biomagnify (e.g. Hall and Kolbe 1980); in fact, it is this property which mainly accounts for the general replacement of DDT with insecticides such as fenitrothion and aminocarb in budworm control programs. Thus, investigations into the potential indirect effects of aminocarb have focused on reductions in food supply and disruption of biocontrol. This has been approached by studying the population dynamics of certain non-target species in the spruce-fir forest. A major obstacle is that the population dynamics of most non-target species are very poorly understood. Population trends, both seasonal and perennial, are regulated by a variety of powerful natural factors, viz weather, food supply, disease, dispersal, habitat, etc. As well, activities such as pesticide application may significantly affect the dynamics of some populations. The challenge in the spruce-fir forest has been to determine the degree to which fluctuations in numbers are attributable to the spray program, as opposed to natural factors. Because of the absence of baseline data on population dynamics of most species, this is a difficult and complex challenge.

The value of such field studies has always been seriously undermined by the general absence of baseline data, and by the plethora of unanticipated events which traditionally plague field experiments conducted in association with forest spraying operations. Problems associated with weather, aircraft guidance, mechanical performance of the aircraft, changes in operational spraying plans, field communication, etc. are the rule, rather than the exception, in operational spraying programs (Varty 1976, 1980). As well, the statistical validity of differences observed in environmental monitoring data is usually unknown, due to lack of replication and/or insufficient sampling of the community being studied. Nevertheless, even with these deficiencies, a large number of investigations and monitoring programs have been completed. These investigations, taken individually, have rarely been conclusive, but taken collectively, the data have provided consistent indications of the nature and magnitude of the hazard posed to certain non-target species. Clearly, however, there is a critical need for well-designed field studies to gather baseline data on selected indicator species, as well as to determine the effects of spraying on these species.

Several studies relating to the chemical persistence of aminocarb, and the spatial and temporal synchrony of aminocarb and non-target species have contributed to an understanding of ecosystem vulnerability. The amount of chemical released into the forest during spraying, the nature of its formulation,and the acute toxicity of the chemical(s) to non-target species are important factors. Aminocarb is currently applied at 70 to 87 g active ingredient per hectare ($g\text{-}AI.ha^{-1}$). The vulnerability of a species is affected by how closely the activity of

the species in synchronized with the timing of the spray program. For example, McLeod and Mortensen (1975) found that colonies of honeybees placed within an area sprayed in mid-May (with fenitrothion or mexacarbate) experienced no increase in mortality, whereas spray application 3 weeks later resulted in significant mortality one and two days postspray. The difference in vulnerability was related to the fact that in mid-May, flower bloom, and therefore honeybee activity, were minimal, whereas 3 weeks later, flowering was common and adult bees were actively foraging.

Seasonal differences in vulnerability have also been documented by Plowright and co-workers. Two bumblebee species, Bombus terricola and B. ternarius, which emerge early in the spring, are more vulnerable and populations are greatly reduced by spraying (Plowright et al. 1978). However, species which emerge from hibernation late in the spring, after the spray programs, are apparently unaffected by spraying. Thorpe (1980) observed the same phenomenon with solitary bees; early-emerging species (mostly andrenids and halictids) are actively foraging when spray residues are high, and are highly vulnerable; late-emerging species (the colletid, anthrophorid and megachilid species) are much less vulnerable. The effects of aminocarb on pollinators are discussed in detail in Section 4.2.2.4.

Similarly, entomophilous plant species which bloom during spraying programs are potentially vulnerable due to reductions in pollinator insects (Plowright 1980).

Even diurnal behavior patterns can effect the vulnerability of a non-target species. Forest spraying programs against spruce budworm are generally conducted in the early morning (0430 to 0800 h) or evening (1930 to 2200 h). Some invertebrate species are most active during the warm midday period and therefore, are not as vulnerable to the insecticide as species which forage actively at dawn (Thorpe and Varty 1978).

Spatial variability in pesticide deposit also affects vulnerability of various non-target species. The exposure of various forms of wildlife to aminocarb depends on the degree to which they are protected from spray deposit as well as on their mobility and feeding habits.

The forest canopy intercepts the great majority of aerially-applied insecticide. Generally, the inner crown of a tree, which does not support the budworm but does support non-target organisms, may receive 20 to 50% as much deposit as the outer crown (Armstrong and Yule 1978), on which the budworm feeds. These non-target organisms are subject to a potential hazard. For example, insectivorous birds that inhabit the upper crown canopy could be subjected to a relatively high pesticide exposure by several routes, e.g. inhalation of vapors as they fly through the spray cloud, absorption of residues through their feet, preening of residues from their feathers or ingestion of intoxicated prey.

Monitoring of spray deposit in operational programs has repeatedly shown that, within a forest stand, generally less than 10% of the emitted insecticide filters through the canopy and reaches ground vegetation, where many non-target species, such as bees and small herbivorous mammals, are active (Buckner et al. 1975; McLeod and Mortensen 1975). Thus, invertebrates and wildlife species in fully exposed habitats, e.g. clearings, roads, rights-of-way, are much more vulnerable than those under the forest canopy, and indeed experience greater mortality (Plowright et al. 1978).

While organophosphorus and carbamate insecticides are considered short-lived, there is mounting evidence that parent compounds or their primary metabolites persist for a surprisingly long time in certain strata within the spruce-fir forest (see Section 2.7). As noted, the persistence of aminocarb in balsam fir foliage (at 0.017 to 0.037 $mg.kg^{-1}$) one year after application (Barnes 1980) may be of particular concern. No insecticidal effect of these aminocarb residues has been investigated but McNeil and McLeod (1977) have shown such a phenomenon for fenitrothion. Residues of fenitrothion or its metabolites persisted for more than a year in jack pine foliage inadvertently sprayed in a spruce budworm spray program. These residues, which ranged from below detection limits to 0.35 $mg.kg^{-1}$ (depending on the analysis), were sufficiently high to result in 36 to 68% mortality (corrected for natural mortality) of Swaine jack-pine sawfly larvae, Neodiprion swainei, which fed on the foliage. Thus, in areas repeatedly treated with aminocarb, residues may persist which might be lethal to some insects feeding on foliage of coniferous tree species, albeit fenitrothion and aminocarb are quite different classes of compounds.

4.2 EFFECTS OF AMINOCARB ON NON-TARGET INVERTEBRATES

4.2.1 DEVELOPMENT OF RESISTANCE AND SECONDARY PESTS

Two disadvantages of the repeated and widespread use of the same class of insecticides, especially in the agricultural sector, have been the development of resistance in the target species and outbreaks of minor, secondary pests due to insecticide-induced disruption in biological control processes. Resistance can be anticipated to develop more rapidly if:

a) the dispersal capacity of the insect pest is limited;
b) the same class of chemical insecticide is used in the same area against each generation of the insect;
c) the mortality rate achieved with the insecticide is very high, i.e. 95%;
d) certain classes of insecticides, e.g. cyclodienes, are used;
e) there is more than one generation of the insect each year.

A review of the conditions under which aminocarb is used, in relation to the above factors, indicates that resistance is unlikely to develop in the spruce budworm.

Investigations of the dispersal of budworm moths have established that significant components of the adult female population migrate for distances of 70 to 300 km (Greenbank et al. 1980) after mating, and therefore distribute their eggs widely. Thus, there is great opportunity for exchange of moths and genetic material between the sprayed areas and unsprayed area.

Although budworm spray programs cover a large geographic area, they represent a very small proportion of the total budworm outbreak. For example, the 1980 outbreak of spruce budworm in eastern Canada covered 36.2 million hectares; within that area, only 1.85 million ha (5%) were sprayed, and only 279,800 ha (<1%) with aminocarb. Futhermore, the sprayed area is composed of discontinuous blocks, distributed throughout five eastern provinces and the state of Maine. Although some blocks are treated annually, many are sprayed irregularly over a period of several years. In analyzing the spray history of several locations in New Brunswick from 1971 to 1974 inclusive, Eidt and Fisher (1982) found that of 547 points sprayed in 1971, 7% were sprayed for 3 consecutive years, 50% were sprayed 2 of the 4 years, and the balance (43%) were sprayed only 1 year in 4.

Since 1965, a variety of products, representing four classes of insecticides (organochlorines, organophosphorus compounds, carbamates and microbials), have been used operationally, viz DDT, phosphamidon, fenitrothion, aminocarb, carbaryl, mexacarbate, trichlorfon, acephate, and Bacillus thuringiensis (Nigam 1980). Use of a variety of insecticides mitigates against the development of resistance. A low level of resistance to organophosphorus insecticides may be anticipated after 45 generations of treatment (Harris and Svec 1976). In contrast, the use of cyclodiene compounds induces resistance after only 20 generations. Resistance to carbamates (although examples are scarce), is expected to develop at a rate similar to organophosphorus compounds, i.e. after about 45 generations (Harris 1981).

In the case of the spruce budworm, one spray program is conducted each year because the budworm is univoltine (one generation per year). In agricultural or structural pest control programs, mortality rates generally exceed 90%, and often 95%. In budworm spray programs, budworm mortality seldom exceeds 90% and frequently is less than 80%. The above factors indicate that the selection pressure on spruce budworm from aminocarb use is relatively low. Resistance to aminocarb is unlikely to develop, provided the current use-pattern is maintained.

A common indicator of resistance is a trend towards increasing rates of application in order to achieve the same level of efficacy. No

such increase in the dosages of aminocarb applied by the various provinces in the past decade is apparent. However, it is highly doubtful that the methods used to assess efficacy are sufficiently sensitive to detect the development of resistance. Moreover, aminocarb has not been used long enough for evidence of resistance to appear.

Mortality of a wide variety of aerial insects, including beneficial species, is an unavoidable consequence of current spraying with broad-spectrum insecticides. Disruption of the predator-parasite complex through spraying sometimes results in outbreaks of insects of secondary importance, previously held in check by the predator-parasite complex. Widespread spraying has been conducted annually in New Brunswick for about 30 years. Throughout this period, outbreaks of several minor insect pests (e.g. lesser maple spanworm, tussock moth, saddled prominent moth, birch sawfly and spruce coneworm) have occurred but have been reported to be as severe in unsprayed districts as in sprayed areas (Varty 1976, 1978).

In conclusion, it seems unlikely that continuation of the current use-pattern of aminocarb in forest spraying will induce resistance in the spruce budworm. Similarly, there is no evidence that aminocarb, as used in Canadian forestry, has induced outbreaks of any secondary insect pests. It seems unlikely that continued sporadic use of aminocarb will induce such outbreaks.

4.2.2 EFFECTS ON BENEFICIAL INVERTEBRATES

The repeated use of some chemical insecticides is generally recognized as having a disruptive effect on the natural dynamics of various beneficial invertebrate populations. The disruptions associated with large scale aerial spraying programs against the spruce budworm have been investigated for more than 20 years, and thus some of the overt immediate effects of the operational use of insecticides, viz DDT, phosphamidon, fenitrothion, and aminocarb, on many beneficial insect species in the spruce-fir ecosystem are reasonably well understood.

As mentioned previously, one serious difficulty in accurately assessing the environmental impact of spraying has been the scarcity of baseline data. The norms in terms of population levels, seasonal trends, cycles, etc. are often very poorly understood. Such is not always the case; the work of Morris and colleagues (Morris 1963) has provided a good information base regarding the behavior and rates of parasitism and predation of many species, and the effect of these activities on spruce budworm survival and population dynamics.

Those species which have emerged and are active at the time of insecticide spraying are the most vulnerable to damage. They include bees, spiders, ants, parasites of budworm larvae, and some soil invertebrates. The gross effects of formulated aminocarb on the invertebrate

community have been monitored using a variety of trapping techniques (Malaise, sweep net and pitfall) which are intended to detect large changes in total numbers of invertebrates and/or relative abundance of various taxa. However, the techniques used all have limitations, which reduces the value of much field data. Malaise and pitfall trapping are considered relatively useless for the quantitative assessment of invertebrate populations (Southwood 1966; Varty 1980). Their usefulness may be limited to collecting specimens and detecting changes in the species diversity of a community. Although sweep netting is used to estimate numbers, the sampling error is considerable, and thus it can be used to detect only very large fluctuations in numbers (NRCC 1981).

In Maine, numbers of Ichneumonidae were reduced one week after spraying with formulated aminocarb at 168 g-AI.ha^{-1} (Brown 1978) but it was reported that these populations had recovered their numbers by one month postspray. Numbers of Syrphidae may have been temporarily reduced by spraying. A similar program in Newfoundland (Barnes 1979) indicated that formulated aminocarb spraying had no significant effect on a variety of invertebrate orders, including Hemiptera, Homoptera, Hymenoptera, Diptera and Coleoptera. These observations are of questionable significance because of the above-mentioned limitations in the sampling methods.

In a preliminary report, Millikin (1981) described the relative impact of aminocarb 1.8D and 1.8F formulations on a variety of terrestrial invertebrate orders. Millikin collected specimens from sampling buckets under balsam fir, in sprayed and unsprayed areas, a technique with the limitations mentioned above. There was at least an average twofold increase in knockdown, over a 3 d period, following application of aminocarb 1.8F (70 g-AI.ha^{-1}, formulated with Atlox and water or with diluent 585). Orders affected included Coleoptera, Diptera and Hymenoptera as well as Lepidoptera (spruce budworm). Application of aminocarb 1.8D (70 g-AI.ha^{-1} formulated with diluent 585) caused a large (up to 100-fold) increase in knockdown of Coleoptera over the 3 d period following spray, but only slightly increased knockdown of other species on the day of spray. It was not possible to evaluate the statistical significance of any of these data. The data suggest that the flowable aminocarb formulation may have a slightly more severe impact on some orders of terrestrial invertebrates than does the 1.8D formulation.

4.2.2.1 Larval and Pupal Parasitoids

The major parasitoids of spruce budworm larvae and pupae fall into three categories:

a) overwintering parasites of larvae, Apanteles fumiferanae Vier. and Glypta fumiferanae Vier.;

b) parasites attacking large larvae, Meteorus trachynotus Vier. and several Diptera;
c) parasites attacking pupae, mainly Ephialtes ontario (Cress.), Itoplectis conquisitor (Say) and Phaeogenes hariolus (Cress.).

Most of the early data on parasite abundance relate to insecticides other than aminocarb (e.g. DDT, fenitrothion). Although the mode of action in which different insecticides affect parasites is not known and the characteristics of DDT and aminocarb are quite different, earlier data can be used to illustrate the types of effects one might anticipate with aminocarb use.

Based on sampling conducted in the 1950s, Macdonald and Webb (1963) suggested that the abundance and parasitism rates of the major larval and pupal parasites of spruce budworm were affected by DDT spraying programs. They stated that parasitism by most major species, measured as the percentage of spruce budworm parasitized, appeared higher in sprayed areas than in unsprayed areas in the year of spraying. Multi-year monitoring of parasitism by Apanteles and Glypta during the 1970s (Varty 1977) indicated no general trends in percent parasitism as a result of spraying with fenitrothion. A summary of a multi-year survey (1976-1979) of the Maritime provinces, reported that rates of parasitism of budworm were not drastically adversely affected by the annual spraying program (Magasi et al. 1980). According to this report, none of the insecticide regimes, including formulated aminocarb, caused a drastic reduction in rates of parasitism. Indeed, percent parasitism of residual budworm populations in sprayed areas appeared higher. This monitoring program involved annual collection of budworm larvae from several plots using the same plots each year, dissection of larvae, identification of the parasite species and calculation of percent parasitism. Collections were made from sprayed and unsprayed areas before and after spraying.

Several authors (Miller 1963; Varty 1977; Magasi et al. 1980) have pointed out limitations to the inferences that can be drawn from data on rates of parasitism:

a) They are a measure only of percent parasitism of budworm larvae, not of parasite numbers or of parasite mortality. Large numbers of parasites could be killed by spraying without these reductions being reflected in percent parasitism.

b) In the case of parasitism by Apanteles and Glypta, larvae were parasitized approximately 10 months before spraying; thus it may be incorrect to infer that the rate of parasitism could be meaningfully altered by spraying occurring several months later. However, if there are behavioral differences between parasitized and healthy budworm larvae, the insecticide could discriminate within the population (Varty 1982).

c) Examination of Macdonald and Webb's (1963) data for 1, 2 and 3 years postspray (mainly with DDT) indicates that adverse effects may not

appear until later. Parasitism by Apanteles and Meteorus appeared higher in the year of spraying but was lower 2 and 3 years postspray. Parasitism by Glypta was lower in the year of spraying and 2 and 3 years postspray. This delayed effect may have resulted from the highly persistent nature of DDT, and may not occur with less persistent chemicals, such as aminocarb.

d) Parasitized larvae are thought to have different photic reactions than unparasitized larvae (Lewis 1960) and because of this, their exposure to aerially-applied insecticide is less. Thus, the differential vulnerability of parasitized larvae, in itself, may result in higher parasitism rates of larvae which survived spraying. In fact, Hamel (1977) demonstrated that parasitism by Apanteles and Glypta was significantly higher in blocks treated with the microbial insecticide, Bacillus thuringiensis (B.t.), (which does not affect non-lepidopteran insects) than in untreated blocks. A similar increase was noted for Apanteles and Glypta following spraying with B.t. plus acephate in Newfoundland, although the significance of the increase was not noted (Otvos and Raske 1980). Regardless of the nature of the effect, attempting to determine whether parasitism rates are directly affected by spraying is seriously complicated by the behavioral differences of parasitized larvae.

The foregoing factors impose serious limitations on the inferences that can be drawn from data on rates of parasitism. Varty (1977) has summarized these difficulties as follows: "Percent parasitism values must be interpreted with caution. Rising or falling values of parasitism between years reflect changes in the relationship between host number and parasitoid number; they do not necessarily indicate a similar rise or fall in the absolute population of parasitoids in the sample plot. Declining values of percent parasitism indicate a real reduction in parasitoid abundance only when the host population is static or lower between years. Percent parasitism may also decline when the absolute population of parasitiods is increasing provided the host populations are increasing even faster."

In addition to these limitations in the method, a review by the panel of the field data collected in the Maritime survey (Magasi 1981; summarized in Magasi et al. 1980) revealed several factors which make it difficult to draw conclusions about the significance of the observed effects of spraying on parasitism. The sprayed areas were treated with Dylox (trichlorfon) and/or fenitrothion and/or aminocarb over the course of the study. Some of the control plots also had a past spray history. The authors were trying to assess only gross impact, rather than subtle changes and their conclusions (Magasi et al. 1980) are based on percentages calculated from the sum of budworm and parasite counts in all the plots studied. The methods used make it difficult to draw any conclusions about other than catastrophic changes. However, an analysis by the panel of the raw data from the Maritime survey (Magasi 1981) indicated that there may be decreases in percent parasitism by

certain specific parasite species in plots sprayed only with aminocarb. The long-term implications of this are unknown. The panel considers that the important question is not whether parasitism of a population of budworm larvae that has been sprayed is significantly affected, but whether the parasite population remaining after spraying is sufficient to produce normal parasitism rates in the next generation of budworm larvae. Thus, between-generation comparisons of parasitism should be used to assess the adverse effect of spraying programs.

4.2.2.2 Egg Parasitoids

Parasitism of budworm eggs by Trichogramma minutum is an important factor in budworm survival. In the early 1950's, egg parasitism ranged from 0 to 10% (Miller 1963). The recent survey of the Maritime Provinces showed that egg parasitism was generally higher than in the 1950's; there was no evidence that egg parasitism was reduced by spraying with insecticides, including formulated aminocarb. However, the limitations outlined above may also apply to data on egg parasitism.

T. minutum parasitizes the egg stage of a wide variety of lepidopterous insects. The Trichogramma population in an ecosystem sustains itself by sequentially parasitizing various insect hosts including spruce budworm. Spraying does not appear to affect parasitism of budworm eggs in midsummer, however parasitism of alternate host insects at the time of spraying may logically be reduced by spraying. This possibility does not appear to have been investigated.

4.2.2.3 Predaceous Insects

In the balsam fir component of the spruce-fir forest, the predominant predaceous insects include various Hemiptera (Miridae, Anthocoridae, etc.), Coccinellidae, Cecidomyiidae (midges), Syrphidae, Chrysopidae and Carabidae as well as mites, spiders, harvestmen and ants (Varty 1980). Of these, spiders are regarded as the most important in influencing the dynamics of arthropod species in the boreal forest, including spruce budworm.

Forest spraying with insecticides, including formulated aminocarb, appears to affect predaceous insects. Increases in population densities of Coccinellidae and declines in population densities of several predator families, i.e. Syrphidae, Pentatomidae and Chrysopidae, as well as spiders, were noted in association with DDT spraying nearly 20 years ago (Macdonald and Webb 1963). The higher rates of coccinellid density persisted in postspray years while other predator populations declined in the year of spraying and took one to two years to recover. Recently, Plowright (1980) noted that formulated aminocarb caused significantly increased mortality of Syrphidae, but did not affect Bombyliidae, another family of Diptera. The fruit-set of two

plant species pollinated by syrphid flies, Maianthemum canadense and Cornus stolonifera, was also significantly reduced in aminocarb-sprayed areas.

Spraying with formulated aminocarb (2 x 70 g-AI.ha^{-1}) may result in heavy mortality of spiders. In three years of spraying (1977 to 1979) using the same experimental block, the total mortality of spiders ranged from 37 to 66% following the first application and from 66 to 69% following the second application (Varty 1980, 1981). The degree of mortality differed considerably between species. One web-spinning species, Theridion murarium, which inhabits the apical shoots which intercept much of the spray, experienced 94% and 96% mortality in 1978 and 1979, respectively (Varty 1980, 1981) and some species apparently suffered even higher mortality. The common hunting spider, Metaphidippus flavipedes, suffered 21% to 36% mortality in the same years on the same trees (Varty 1980, 1981). Despite the acute effect of formulated aminocarb on spiders, seasonal sampling indicated that numbers recovered to some extent although the mechanism of recovery could have been immigration and/or local regeneration. A 4-year survey showed that spider population trends from 1977 to 1980 were parallel in aminocarb sprayed and unsprayed areas, but peak total densities were consistently lower in the aminocarb area than in the unsprayed area, although not as low as one might expect from the mortality experienced with spraying (Table 4-1) (Varty 1980, 1981).

Because some spider species are more susceptible to insecticides than others, one might suspect reduced species diversity in an area subjected regularly to insecticide application at rates high enough to induce effects. Data presented in a summary report (Varty 1980) indicates that in fir crowns in an area with a long and frequent spray history (with DDT and fenitrothion), the number of spider species is considerably lower than in unsprayed areas. The long-term implications are unknown.

Varty (1980) concluded that it is too early to show whether aminocarb affects spider species dominance and diversity. One study (Varty 1982) indicates that an area treated with aminocarb in 1977 through 1980 showed lower species diversity only in 1978 when compared with the control area (21 compared with 22 species in 1977, 18 compared with 26 species in 1978, 27 compared with 30 species in 1979 and 32 compared with 28 species in 1980). The aminocarb-treated stand appeared to maintain its species diversity over the 4-year period. It is difficult to interpret these data because the aminocarb plot was also sprayed with DDT and fenitrothion prior to 1977. A much broader survey, on areas with no previous spray history, would be needed to assay the impact of aminocarb on spider species.

In summary, formulated aminocarb applied at operational rates against spruce budworm resulted in high levels of spider mortality at a time when they were preying on spruce budworm. However total spider populations appeared to recover quickly from this mortality, and were not significantly depressed over the years of observation.

Table 4-1. Densities of spiders on balsam fir in July (No. m^{-2}) (Varty 1980).

	Number of Branch Samples[α]	Number of spiders per m^2	
		Aminocarb-Sprayed	Unsprayed
1977	100	3.1	5.0
1978	100	9.1	11.3
1979	200	18.6	21.0
1980	200	10.7	11.6

[α] Branch samples (each about 0.25 m^2) were cut in midcrown of 50-100 trees about 10 m tall (Varty 1982).

In addition to spiders, heavy mortality of adult chalcid wasps (60-70%), and moderate mortality of beetles and ichneumonid wasps (40-50%) were reported in association with aminocarb applications (Varty 1978).

Red wood ants are widely recognized as important predators of defoliator larvae. In Canada, studies by Finnegan (1978) have shown that Formica lugubris preys aggressively on the large larval and pupal stages of spruce budworm. Such predation has been effective enough to reduce defoliation of the host trees by 10 to 20%. Some forest insecticides, e.g. fenitrothion (Plowright and Rodd 1980) cause heavy mortality of wood ants. However, the absence of information on the impact of formulated aminocarb on ants indicates that this area of investigation deserves attention.

Some of the invertebrate mortality observed with aminocarb applications may be related to nonyl phenol, a solvent contained in formulated aminocarb. Kingsbury et al. (1981a) applied nonyl phenol at 0.47 $L.ha^{-1}$, a dose equivalent to the amount of nonyl phenol applied in the seasonal maximum permissible dosage of aminocarb (2 x 87 $g\text{-}AI.ha^{-1}$). Their study employed drop trays located on the ground under deciduous and coniferous canopies, as well as colonies of domestic honeybees, in treated and untreated blocks. The numbers of terrestrial invertebrates collected in the drop trays were very small and the statistical significance of the differences observed is unknown. Their data indicated a 5- to 7-fold increase in mortality of Araneida (spiders) and Diptera (flies) under the deciduous canopy, but not the coniferous canopy, of the nonyl phenol treated block. Mortality was elevated for 48 h after spraying before returning to normal levels. Mortality of honey bees was also elevated (ca 4-fold) in the 24 h period following treatment, but returned to normal 48 h posttreatment.

The use of formulated aminocarb causes high levels of mortality in predator populations exposed at the time of spraying. However, most taxa appear to return to near normal population densities in the year of spraying. What remains unknown is the effect of aminocarb-induced mortality on the efficiency of predation on spruce budworm.

4.2.2.4 Pollinators

Pollinator species are of critical importance in the production of domestic and wild fruit, field crops, and honey, as well as the reproduction of a range of plant species. The most important pollinators are social bees and solitary bees. Spruce budworm spraying programs have produced mortality among domestic and native bee populations, and syrphid flies. Studies which examine only kills adjacent to hives do not provide adequate information. The key question is the percentage of active foraging bees killed and ultimately the short- and long-term impact on pollinating activity. A very small kill of the total hive population (e.g. 1%) can be indicative of severe mortality in the foraging component (NRCC 1981). Also, the detection of

dead social bees near hives may be indicative of a more severe problem in wild pollinator populations. Analysis of the problem primarily requires establishing the ecological behavior of bee populations and recognizing that some species may be more susceptible than others (see Section 4.1). For example, mortality of foraging bees is more important to colonies of native bees that it is to domestic bees. In most native bee species, only the overwintering queen bee is foraging at the time of forest spraying; thus the loss of the foraging queen can result in the loss of the colony (NRCC 1981). Of the native bees in the spruce fir forest, solitary bees (e.g. andrenid and halictid species) represent about 90% of the population (Thorpe 1980).

As with other organisms, pesticides may enter bees by any of three routes (oral, dermal, or respiratory). Given the characteristics of forest spraying operations, dermal exposure is probably the major route of entry. The LD_{50} of topically applied aminocarb for honeybees is 1.2 µg per bee (NRCC 1981). Aerial application of a given pesticide is considered to be more hazardous to bees than ground application because aircraft cover large areas rapidly and bees have less opportunity to avoid the spray (NRCC 1981). Another factor which increases the hazard is that because forest spraying is low volume or ultra-low volume, spray droplets or residues have a high concentration of the toxic ingredient. Offsetting this is the observation that liquid formulations and liquid spray applications, such as formulated aminocarb, are less toxic to bees than wettable powders and dust applications.

Besides dermal exposure, toxicity may also result from pesticide-contaminated nectar or pollen, particularly that fed to the young brood inside the hive. However, the relative hazard of aminocarb to bees is reduced by the fact that pollen contaminated with carbamate insecticides is much less toxic to bee larvae than that contaminated with organophosphorus insecticides (NRCC 1981).

In areas where pollinator insects are important, mortality may be reduced considerably by avoiding spraying during the hours of peak foraging activity (NRCC 1981).

The daily foraging pattern differs with the crop and it is clear that in order to avoid significant damage, the daily activity of pollinator species should be monitored in the area, and for the crop of concern, e.g. blueberries. The earliest work on the effect of formulated aminocarb on bees utilized colonies of domestic honeybees placed within the spray block. A 1973 trial in Quebec involved an application of aminocarb (52 g-AI.ha^{-1}, presumably formulated with nonyl phenol and fuel oil) around noon (Kingsbury and McLeod 1978). At this time of day, honeybees are foraging actively in the field and are exposed to both aerially-suspended spray and liquid residues on foliage. Adult honeybee mortality increased dramatically, from 3.d^{-1} prior to spray to 505.d^{-1} one day postspray and 46.d^{-1} two days postspray. This mortality amounted to less than 1% of the colony populations, but it is unclear how high the mortality of the foraging component was. Mortality

rates were normal after 48 h. Activity in the treated hives remained high because bees clustered around the hive entrance but foraging activity was reduced as evident from a decrease in pollen collection. It was not possible to establish the statistical significance of these data. Similar low level mortality was observed in New Brunswick in association with a double application of 70 g-AI.ha^{-1} formulated aminocarb in mid-June (McLeod 1978).

Plowright and co-workers have investigated the effect of aminocarb on bumblebees and solitary bees since 1977. They noted that although most of the mortality attributable to the insecticide occurs within the first 48 h, the sharpest comparisons between treatments are generally obtained by using survivorship at the end of a one-week period (Plowright and Pendrel 1978). They found that aminocarb, applied at operational doses (70 g-AI.ha^{-1}), had no direct detectable effect on bumblebees (Bombus spp.) in exposure cages placed directly under flight paths. With regard to caged solitary bees (andrenid and halictid species), a significantly higher mortality (28%) occurred in aminocarb-sprayed cages set out in fully exposed locations than in the control cages (11%). A later experiment (Plowright and Rodd 1980) also found a significant effect on caged solitary bees; the cages sprayed with aminocarb, in fully exposed locations within 50 m of the nearest flight path, showed 47% mortality compared with 10% in the control cages. These numbers are statistically different ($P > 0.01$). They found no statistically significant effect on caged solitary bees 100 m from the nearest flight path.

In a preliminary report, Kingsbury et al. (1981b) state that the aminocarb 1.8F formulations (oil or water based) do not appear to have a more severe impact on bees than does the 1.8D-diluent 585 formulation. However, all three formulations applied at 350 g-AI.ha^{-1} (4 times the rate used in operational programs) were reported to cause short-term reductions in wild pollinator activity, honeybee colonies caged within aminocarb 1.8F treated plots suffered higher mortality than did control colonies, and there was a decrease in pollen collected from 1.8F treated hives. It was not possible to evaluate the statistical significance of these data.

An interesting secondary effect of aminocarb spraying is also suggested. In whole colony experiments in New Brunswick, Plowright and Pendrel (1978) found that mortality of bumblebees in aminocarb-sprayed areas was lower (18.4%) than in unsprayed areas (43.6%). They suggest that this could be related to the fact that the population levels of spiders, which are recognized as significant predators on bees, are substantially reduced by aminocarb, as was noted earlier.

In summary, aminocarb (as currently formulated) applied at current operational rates (70 g-AI.ha^{-1}, once or twice) has an impact on both honeybees and solitary bees directly exposed to spraying. This mortality appears to be low-level but its significance remains to be determined. No significant impact has been detected on bumblebees.

Three secondary questions arise from bee mortality observed in connection with aminocarb spraying:

i) Does a serious reduction in the fruit-set of insect-pollinated plants result?
ii) Is there an associated decrease in the diversity of plant communities because of the reduction in cross-pollination and presumed increase in asexual reproduction?
iii) Are insect-pollinated plants placed at a competitive disadvantage to wind-pollinated plants?

Plowright et al. (1978) observed no reduction in entomophilous fruit-set associated with aminocarb impact on bees. Thorpe (1980) observed a 42% fruit-set in an aminocarb-sprayed block compared with 54% in the control block, but these numbers cannot be verified statistically. Thaler and Plowright (1980) report that the fecundity of Clintonia and Kalmia (both plants primarily visited by bumblebees) is not adversely affected by aminocarb sprayed at operational rates. Fecundity was actually higher in the sprayed areas, consistent with the observed higher survival rates among bumblebee and workers (Plowright and Pendrel 1978). Thaler and Plowright (1980) point out that plant species pollinated mostly by Diptera and solitary bees would more likely be vulnerable to aminocarb sprays. They state that work to test this hypothesis is now being tested. In a summary report Plowright (1980) states that the fruit-set of two plant species pollinated by syrphid flies, Maianthemum canadense and Cornus stolonifera was significantly reduced in aminocarb-sprayed areas.

4.2.2.5 Soil Invertebrates

The beneficial role of invertebrates in decomposing organic matter and forming soil humus in forests is widely recognized. Complete decomposition is a gradual, stepwise process carried out by a variety of flora and fauna, each with its own role. A reduction in the numbers or efficiency of any of the important taxa could seriously affect decomposition and humus formation.

In the spruce-fir ecosystem, several groups of arthropods contribute significantly to primary decomposition of plant material - beetles, millipedes, ants, mites, springtails and earthworms (Armson 1977). Decomposition of cellulose and lignin is particularly dependent upon a number of fungi - the Ascomycetes, the Basidiomycetes and the Fungi Imperfecti.

Because soil organisms are not highly mobile, their ability to leave or enter insecticide-contaminated areas is limited. This factor greatly increases their exposure and the probability of an adverse effect on decomposition.

Information available on the effect of formulated aminocarb on various soil invertebrate populations is very limited and superficial; there appear to be no data on the effect on fungi. Studies have involved pitfall trapping of soil fauna over a specified time period, and counting of fauna by taxa. In areas with a history of insecticide use (fenitrothion or aminocarb) there is a lower apparent abundance of springtails (Collembola), millipedes, spiders and carabid beetles (Varty 1978). A study in Newfoundland also provided some evidence of reduced populations of springtails in aminocarb-sprayed areas one year after treatment (Barnes 1980). In areas with a long history of spraying with fenitrothion, numbers of carabid beetles and spiders appear to have declined substantially over a 5-year period. Unfortunately, similar long-term historical data on the abundance of various invertebrate taxa are not available for aminocarb-treated areas.

Since decomposition is of such great importance in nutrient cycling in the boreal forest, the effect of repeated aminocarb applications on decomposer organisms and decomposition should be investigated. The effort should be directed to selected indicator groups, e.g. mites, nematodes, ants and fungi. Data on postspray residues and persistence of aminocarb and its toxic metabolites in the organic layer of forest soil are being generated, but without information on the availability of these chemicals and on species toxicity, it is impossible to determine the hazard posed by these residues (Barnes 1980).

4.3 EFFECTS OF AMINOCARB ON WILDLIFE

4.3.1 BIRDS

Toxicity data (LD_{50} and LC_{50}) determined from laboratory trials on birds are summarized in Table 4-2. Aminocarb is more toxic when administered in acute oral doses (LD_{50}) than when smaller amounts are received in the diet over a period of time (LC_{50}), because of the ability of birds to metabolize small amounts ingested with the daily intake of food.

The maximum potential dietary intake of aminocarb by insectivorous songbirds can be estimated by combining residues expected in invertebrate prey, assuming no metabolic breakdown, with estimated daily rates of food intake. In the absence of residue data, the concentration of aminocarb in budworm can be estimated as 40.2 $mg.kg^{-1}$. This value is derived by assuming that third and fourth instar (50:50 ratio) budworm larvae have an average body weight of 1.36 mg (Armstrong 1981), receive a deposit of 0.007 $\mu g.mm^{-2}$ on the upper surface of their bodies (assuming uniform distribution of an aerial application of 70 $g\text{-}AI.ha^{-1}$,

Table 4-2. Acute and subacute toxicities of technical aminocarb to birds.

Species	Vehicle of administration	LD_{50} ($mg.kg\text{-}BW^{-1}$)	LC_{50} ($mg.kg\text{-}diet^{-1}$)	Reference
Ring-necked pheasant				
10 days old	diet	-----	200	Hill et al. (1975)
3-4 months old	gelatin capsule	42.4	----	Tucker and Crabtree (1970)
Mallard				
10 days old	diet	----	2552	Hill et al. (1975)
8 months old	gelatin capsule	22.5	----	Tucker and Crabtree (1970)
adult male	propylene glycol	15	----	Lamb and Jones (1975)
adult female	propylene glycol	13	----	Lamb and Jones (1975)
Bobwhite				
15 days old	diet	----	>1000	Lamb and Jones (1975)
adult male	propylene glycol	31	----	Lamb and Jones (1975)
adult female	propylene glycol	41	----	Lamb and Jones (1975)
Starling[a]	propylene glycol	212	----	Schafer (1972)
Red-winged blackbird	propylene glycol	50	----	Schafer (1972)
Domestic chicken	propylene gylcol	75	----	DuBois (1962)

[a] Regurgitated doses readily (Decino 1963)

100%[α] of which is intercepted by the foliage and budworms of the upper third of the canopy) and have a mean measured upper surface area of 8.4 mm^2 (Armstrong 1981). If a 10-g bird is chosen as being representative of upper canopy species, including kinglets and warblers (Nice 1938; Stewart 1937), the mean daily intake of prey would be about 60% of the body weight, or 6 g (Kenaga 1973; Nice 1938); thus, the predicted worst-case daily intake of aminocarb would be 241 µg. This value is close to the lethal oral dose (307 µg) for a 10-g bird, based on a mean LD_{50} of 30.7 $mg.kg\text{-}BW^{-1}$ for four species of birds (Table 4-2). While this exposure might represent a worst-case situation, levels in budworm could be even higher if they ingest contaminated foliage before dying. However, levels in budworms could be lower if they were inside buds and protected from direct exposure to spray.

The dermal toxicity of aminocarb for wild birds has not been reported. This route of exposure could be expected to be quite significant to small, active birds such as kinglets and warblers that perch frequently in the foliage of the upper canopy while feeding. It is difficult to estimate the potential dermal exposure. For a first approximation of the worst-case situation, the concentration of aminocarb impinging on a surface could be 0.7 $\mu g.cm^{-2}$ (assuming uniform distribution of an application of 70 $g\text{-}AI.ha^{-1}$). If the exposed area of a 10-g bird was 48 cm^2[β], the bird could receive a dermal exposure of 3.4 $mg.kg\text{-}BW^{-1}$. In actual fact, the bird would be protected somewhat by feathers, leaves, etc. However, this calculation excludes any residues absorbed through the feet. Fowle (1972) found that songbirds absorbed lethal doses of the organophosphate, phosphamidon (which is considerably more toxic to birds than aminocarb), through their feet when exposed to wooden perches and foliage treated with doses similar to deposits resulting from aerial application. Birds hit by spray might ingest a significant amount of aminocarb while preening; this would add to the oral exposure.

It has been mentioned that even under optimum conditions, local deposition of aminocarb may vary considerably (Carrow 1974). It

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[α] The computer model (Appendix III) predicts that 11% of the aminocarb mass is deposited in the upper 25% of the tree height. Symons (1977) measured a 40% deposition of aerially applied insecticides on the ground in open areas and states similar deposition might be expected in the upper canopy. The assumption of 100% is therefore a likely overestimate but is used here to represent the worst-case situation.

[β] The surface area of birds can be estimated: surface area (cm^2) = $K.W^{0.667}$ (Meeh 1897) where K = 10.4 (Rubner 1902) and W is the weight (g).

is thus imperative that the slope of dose-response curves, as well as LC_{50} and LD_{50} values, be considered in establishing safety factors for the use of aminocarb. If the slope of a dose-response curve is steep, relatively small variations in dose, due to uneven deposition or other factors, may cause a sharp increase in the toxic response of organisms inhabiting the areas receiving a higher than average dose.

There are no reports available on the inhalation toxicity of aminocarb to birds. However, calculation of the potential for upper canopy songbirds to inhale toxic doses of aminocarb from an aerially applied spray cloud is useful. A time-integrated concentration of 2.6×10^{-8} g.s.cm^{-3} in the upper canopy following aerial application at 70 g-AI.ha^{-1} was calculated (Appendix III). A 57-g bird in flight, having a respiratory rate of 1.01 ± 0.03 L.min^{-1} (Berger et al. 1970), could inhale approximately 6.1×10^{-7} mg.kg-BW^{-1} of aminocarb in about 3.5 min at the spray line, assuming 100% of the spray mass is inhalable. There is little information on the influence of the droplet size spectrum on the movement of droplets down avian respiratory systems but the above is likely an overestimate (see Chapter 3). If only 0.5% of the spray mass resides in particles that are small enough to be deeply inhaled, the inhalation exposure would be 3.05×10^{-9} mg.kg-BW^{-1}. Exposure might be greater for a smaller bird with a higher respiratory rate.

Even when the combined detoxification that might occur in the budworm prey and in the birds is considered, the dietary exposure is of the greatest concern. The total (excluding residues absorbed through the feet or ingested while preening) estimated exposure, for a 10-g crown canopy bird, is 27.5 mg.kg-BW^{-1}, close to the LD_{50} reported for several species (Table 4-2).

There is little information available on the sublethal effects of aminocarb on birds. Schafer and Cunningham (1972) suggest that aminocarb could be used as an avian immobilizing agent. They found aminocarb immobilized starlings and red-winged blackbirds at 38 and 50 mg.kg-BW^{-1} respectively, when temporary immobilization was defined as "the point at which a bird lost complete control over wing and leg movements". Both these doses are less than the respective LD_{50}'s.

Aminocarb was included at 3 dose-levels (100, 200 and 800 mg.kg-diet^{-1}) in the daily diet of 3 generations of single comb white leghorn hens (Robinson 1968). For the first 4 weeks of life the P_1 generation animals received basal diet; treatment was then started by incorporating the test material in the diet. A second nonspecified compound was tested concurrently. Each group (2 control and 3 treatment) consisted of four cockerels and 20 pullets. The following parameters were recorded from the parent and F_1 and F_2 generations: general conditions, mortality, body weight, food consumption, efficiency of food utilization, egg production, time to reach maturity, egg whites, fertility, hatchability, embryonic abnormalities and gross pathology.

Additional information was obtained from the F_2 generation; 6 females and 4 males were subjected to detailed gross pathological examinations, organ weight and histopathology.

Signs of aminocarb toxicity were seen in the high dose, 800 mg.kg-diet^{-1}, pullets of the F_1 and F_2 generations. They appeared to be less active and showed an altered behavioral pattern. A significantly elevated mortality rate during the 33 d after hatching was observed in the high-dose groups, F_1 generation. Aminocarb (800 mg.kg-diet^{-1}) significantly affected the weight gain in all three generations and also reduced the food consumption slightly. Aminocarb also delayed maturity in the highest dose groups in all generations. The egg production per bird was consistently lower in the high-dose groups than in any other group and egg size in the F_1 generation was significantly smaller in the high-dose group. In the F_1 generation, the fertility of the eggs was significantly lower in the low- and high-dose group. The hatchability of the eggs was not significantly influenced by treatment and no effect on organ weights was observed. Histopathology was not indicative of treatment related pathological lesions. Pathological observations of the embryos were insufficient for an evaluation of embryotoxic or teratogenic effects. From these results it can be concluded that aminocarb fed to hens at a dietary level of 800 mg.kg^{-1} retarded growth, delayed sexual maturity and reduced egg production. Dietary levels of 100 and 200 mg.kg^{-1} aminocarb over 3 generations did not affect the parameters measured in this study. Therefore 200 mg.kg-diet^{-1} can be considered a no-effect level.

As discussed in Section 5.4, aminocarb did not induce any neurotoxic symptoms in the adult hen at doses up to 2000 mg.kg-diet^{-1} (Kimmerle 1965).

4.3.1.1 Field Monitoring

Field census techniques for birds have an unavoidable, built-in, negative bias which tends to underestimate possible effects (Pearce 1968). For example, effects resulting in behavioral changes may increase the susceptibility of exposed birds to predation and thus the sick bird might be eaten before it is detected in the census. Similarly, scavengers may remove the carcasses of dead birds before they are detected by the researchers. It is therefore quite possible that dead birds will be found only if the impact of a spraying program is catastrophic. Also, the timing of the spray program is such that bird population fluctuation could be masked by migration (Pearce 1968). Many monitoring studies assay bird song as an indication of numbers and activity of birds. It is not clear how the sensitivity of this assay relates to impact; there have been few statistical analyses of this type of monitoring data.

Monitoring studies should also consider that sensitivity may vary with species size. Small, active, upper canopy birds such as kinglets and warblers are most likely to suffer adverse effects from spraying and, as such, may be monitored as indicator species.

It is also imperative to remember that population and ecosystem level responses can be more dramatic than those detected at an individual level. Some species may be particularly sensitive because of an interaction between their life cycle and the timing of the spray program (e.g. migrating or reproductive periods). Certain species may have such critically low population numbers (e.g. endangered species) that even a very small percentage increase in mortality could be crucial in terms of the stability of a species.

Experimental and operational applications of aminocarb have been monitored for effects on forest songbirds since 1970 (Table 4-3). Single applications of 52 g-AI.ha^{-1} (Buckner et al. 1973; Kingsbury and McLeod 1979), 63 and 87 g-AI.ha^{-1} (MacCallum 1980), 105 g-AI.ha^{-1} (Pearce 1971) and 168 g-AI.ha^{-1} (Brown 1978) produced no discernible effects on numbers of singing males during June, when migrants had returned and were defending territories. Germain and Tingley (1980) reported a possible impact of single applications of 70 g-AI.ha^{-1} and 85 g-AI.ha^{-1} on populations of ruby-crowned kinglets (Regulus calendula), Tennessee warblers (Vermivora peregrina), magnolia warblers (Dendroica magnolia) and white-throated sparrows (Zonotrichia albicollis) at one of five locations (Harcourt) monitored in New Brunswick. There were, however, differences in habitat between the control and Harcourt plots that the authors felt were partially responsible for apparent differences. Peterson (1976) found no decreases in brain cholinesterase activity of evening grosbeaks (Hesperiphona vespertina) and American redstarts (Setophaga ruticilla) 24 and 48 h after aerial application of 168 g-AI.ha^{-1} in Maine.

Of the eight reports on the effects of double applications of aminocarb on songbirds (Table 4-3), only two concluded that avian populations had been impacted. The first application of 52 g-AI.ha^{-1} on June 4 near Parent, Quebec, was followed by reductions in numbers of ruby-crowned kinglets; black-throated green (Dendroica virens) and mourning (Oporornis philadelphia) warblers disappeared entirely. The second application of 52 g-AI.ha^{-1} on June 15 was followed by declines in populations of Nashville and magnolia warblers (Buckner and Sarrazin 1975). In New Brunswick, a double application of 70 g-AI.ha^{-1} on July 5 and 7 resulted in a slight 1-day depression of songbird activity the day after the second application on two census plots. The depressed activity was considered to be due to the insecticide because birds on the control plot did not exhibit the same effect and because immature purple finch (Carpodacus purpureus) inside the treated area showed signs of pesticide intoxication (Buckner et al. 1976). A third application of aminocarb (70 g-AI.ha^{-1}) on July 9 did not detectably affect songbird activity. Although the authors of two reports of double applications of

Table 4-3. Synopsis of results of monitoring aerial applications of aminocarb for effects on songbirds.

Year	Location	Spray Regime ($g\text{-}AI.ha^{-1}$)	Effects on singing	Reference
1970	New Brunswick	aminocarb(87)+aminocarb (87)	reduced	Pearce (1970)
1971	New Brunswick	aminocarb (105)	no change	Pearce (1971)
1972	Quebec	aminocarb(52)	no change	Buckner et al. (1973)
1973	Quebec	fenitrothion(140)+aminocarb(52)	reduced	Buckner et al. (1975)
1974	Quebec	aminocarb(52)+aminocarb(52)	reduced	Buckner and Sarrazin (1975)
1975	New Brunswick	aminocarb(52)+fenitrothion(175) +aminocarb (52)	reduced	Pearce et al. (1976)
1976	Maine	aminocarb(168)	no change	Brown (1978)
1976	New Brunswick	aminocarb(70)+aminocarb(70) +aminocarb (70)	reduced	Buckner et al. (1976)
		aminocarb(70)+aminocarb(70)	reduced	Buckner et al. (1976)
1976	New Brunswick	fenitrothion(210)+aminocarb(70) +aminocarb(70)	reduced	Pearce et al. (1979)
1976	New Brunswick	phosphamidon(140)+aminocarb(70) +aminocarb(70)	reduced	Pearce et al. (1979)
1976	Quebec	aminocarb(52)+aminocarb(52)	no change	Buckner and McLeod (1977a)
1977	Newfoundland	aminocarb(70)+aminocarb(70) +aminocarb(70)	no change	Buckner and McLeod (1977b)
		aminocarb(87)+aminocarb(87)	no change	Buckner and McLeod (1977b)
		fenitrothion(210)+fenitrothion (210)+aminocarb(70)	no change	Buckner and McLeod (1977b)
1977	New Brunswick	aminocarb(70)+aminocarb(70)	no change	Pearce and Garrity (1981)
1977	Quebec	phosphamidon(140)+fenitrothion (210)+aminocarb (70)	no change	Kingsbury and McLeod (1980)
1978	Quebec	fenitrothion(210)+aminocarb(52) +aminocarb(52)	no change	Kingsbury and McLeod (1980)
		aminocarb(52)+aminocarb(52)	no change	Kingsbury and McLeod (1979)
		aminocarb(52)	no change	Kingsbury and McLeod (1979)
1978	New Brunwick	aminocarb(70)+aminocarb(70)	reduced	Germain and Morin (1979)
1979	New Brunswick	aminocarb(70)	reduced	Germain and Tingley (1980)
		aminocarb(85)	reduced	Germain and Tingley (1980)
1979	Ontario	aminocarb(63)	no change	MacCallum (1980)
		aminocarb(87)	no change	MacCallum (1980)

aminocarb (Pearce 1970; Germain and Morin 1979) concluded that songbirds were not impacted, their data suggest that there may have been some effect. Pearce (1970) reported that population indices on two census routes were essentially the same as those on the control areas until the time of the first application of aminocarb (87 g-AI.ha^{-1}) on June 8 and 13, respectively. At that point, a decline began in singing activity on the sprayed areas that continued through the second application (87 g-AI.ha^{-1}, a week later) and 10 days beyond, while singing in the control areas increased. Similar results were obtained by Germain and Morin (1979), whose data for magnolia and black-throated green warblers show a 10% decline in singing activity after the second application of aminocarb (70 g-AI.ha^{-1}), made 9-10 days after the first application, whereas activity on the control plots increased. These results are described by the authors as untested statistically and "...much in need of further field verification ...". Songbirds were reportedly unaffected by a triple application of aminocarb (70 g-AI.ha^{-1}) on June 17 and 23 and July 1 in Newfoundland (Buckner and McLeod 1977b).

Busby et al. (1982) report that Matacil 1.8F (2 x 70 g-AI.ha^{-1}) had no significant inhibitory effect on brain cholinesterase in forest canopy songbirds.

Data are available from seven reports of monitoring sequential spray operations in which aminocarb was applied after organophosphorus insecticide (see Table 4-3 for rates of application). When a single application of aminocarb at 52 g-AI.ha^{-1} was made to forests near Menjou Depot, Quebec, approximately 2 weeks after a 140 g-AI.ha^{-1} application of fenitrothion, reductions occurred in populations of ruby-crowned kinglets, black and white (Mniotilta varia), bay-breasted (Dendroica castanea), Nashville (Vermivora ruficapilla) and blackburnian (Dendroica fusca) warblers, yellow-throats (Geothlypis trichas), and evening grosbeaks (Buckner et al. 1975). It should be noted, however, that overlapping of spray swaths may have occurred due to difficulties encountered in adapting large aircraft (DC-6) to forest spraying during 1973, the first year that such aircraft were used in Quebec (Randall 1973). In a spray regime of aminocarb/fenitrothion/aminocarb, applied by TBM aircraft (Pearce et al. 1976), the first spraying did not affect the singing activity of birds; the second spraying was followed by a reduction of 17% in activity of canopy species, and the third spraying, a week later, was followed by a further 28% reduction in activity. Although these results suggest a possible additive effect of the two insecticides, there were some species, such as Cape May warblers (Dendroica tigrina) and white-throated sparrows, that increased during the spraying, and there was no control plot for comparison. In a spray regime of fenitrothion/aminocarb/aminocarb applied by TBM (Pearce et al. 1979), the fenitrothion had no affect on singing activity, but the aminocarb applied a week later resulted in declines of 40% in ruby-crowned kinglets, 28% in Tennessee warblers, and 71% in yellow-rumped warblers (Dendroica coronata). The second application of aminocarb did not result in further declines.

A spray regime consisting of phosphamidon (applied by C-46 aircraft) followed by two applications of aminocarb (applied by TBM) was also monitored by Pearce et al. (1979). The phosphamidon resulted in reduced activity of ruby-crowned kinglets, but aminocarb had no further impact. The remaining three reports of aminocarb being applied in sequence after fenitrothion (Buckner and McLeod 1977b; Kingsbury and McLeod 1980) or phosphamidon plus fenitrothion (Kingsbury and McLeod 1980) conclude that there was no impact on songbirds. These spray regimes, carried out in Quebec and Newfoundland, employed DC-6 aircraft, however, unlike the operations in New Brunswick (Pearce et al. 1976, 1979). A comparison of the impacts on songbirds caused by the application of insecticide from DC-6 and TBM aircraft has shown that spraying by TBM reduced the activity of canopy dwellers whereas spraying by DC-6 did not (Pearce et al. 1979).

Bearing in mind the above discussion on the limitations of the sensitivity of monitoring techniques, only relatively minor impacts on the activity of forest songbirds have been detected and only when aminocarb was applied twice or in regimes involving prior application of fenitrothion or phosphamidon. Given the complexities of weather, avian migration, and spray technology, combined with the difficulties involved in locating suitable unsprayed areas for control plots and finding carcasses of poisoned birds, it is not surprising that the data available thus far do not demonstrate a problem at the application rates in use. In view of the fact that in all of the monitoring studies reported, no dead birds have been found and only one possibly intoxicated bird (a purple finch: Buckner et al. 1976) was sighted, any impact that has been detected could have been sublethal. These conclusions are supported by the fact that the same techniques used for monitoring the impact of fenitrothion and aminocarb have shown that fenitrothion, which is comparable to aminocarb in acute toxicity to birds, has caused sporadic incidences of disappearance or mortality of canopy species (NRCC 1975) when sprayed at 2-4 times the rate used for aminocarb. It must be emphasized that only severe impacts would likely be detected using current monitoring techniques. The toxicity and exposure data, considered together, suggest that at least in the worst-case, aminocarb could have some effect on small crown-canopy birds.

4.3.2 MAMMALS

The available data on toxicity of aminocarb to mammals indicate an order of toxicity similar to that demonstrated in birds. Acute oral and dermal LD_{50} values have been determined for several laboratory mammals (Section 5.5). Tucker and Crabtree (1970) determined an oral LD_{50} of 7.5-15 mg.kg-BW^{-1} in mule deer, when aminocarb was administered as crystalline material in gelatin capsules.

Subacute and chronic effects have been monitored in laboratory mammals and will be discussed in Chapter 5. Small mammals have been monitored for effects of aminocarb when it was applied to forested areas in New Brunswick, utilizing a single spray of 105 g-AI.ha^{-1} from the TBM aircraft (Buckner et al. 1973) and in Quebec, utilizing two sprays of 52 g-AI.ha^{-1} applied by DC-6 aircraft (Buckner and Sarrazin 1975). In both studies, there was no indication that aminocarb had influenced the ratio of immatures: adults or the frequency of pregnant females among shrews and rodents relative to control populations 4-6 weeks postspray. Similarly, Brown (1978) found no changes in sex or age ratios of small mammals captured 4 or 8 weeks after application of 168 g-AI.ha^{-1}.

Bider and Bracher (1980) monitored, by means of a sand transect, the activity of small mammals in a forest plot treated aerially with aminocarb at the rate of 175 g-AI.ha^{-1}, which is 2.5 times the rate now registered for use in forestry. Results showed that the activity of most mammals, including red squirrels (Tamiascurius hudsonicus), chipmunks (Tamias striatus), snowshoe hares (Lepus americanus), jumping mice (Zapodidae), deermice (Peromyscus maniculatus), and common shrews (Sorex cinereus) were unaffected by the spray. Activity of weasels (Mustela erminea) increased fivefold from the fifth to the eighth day postspray, perhaps in response to increased foraging on the ground by birds. Red-backed voles (Clethrionomys gapperi) and short-tailed shrews (Blarina brevicauda) showed signs of reduced activity after the spray, possibly due to increased predation by weasels or due to direct effects of the spray. Previously, an application of 168 g of aminocarb per hectare in Maine resulted in significant declines in brain cholinesterase activity of jumping mice (Napaeozapus insignis); 32% at 24 h postspray and 39% at 48 h postspray, a decline of 34% at 48 h in red squirrels, and no effect on deermice (Peterson 1976). Such levels of cholinesterase inhibition in mammals, however, are surprising since most investigators have failed to elicit inhibition of brain cholinesterase by administering of aminocarb to rats in laboratory experiments (Chapter 5).

4.3.3 AMPHIBIANS AND REPTILES

Rick and Price (1974) monitored the effects on frogs and toads of a 105 g-AI.ha^{-1} aerial application of aminocarb in Panasol or summer oil to operational-size blocks of forest in New Brunswick; they reported no effects, as assessed by counts of adults and observations of behavior. A 70 g-AI.ha^{-1} application of aminocarb to a spruce plantation in Ontario (Buckner et al. 1975) did not visibly affect the survival or behavior of enclosed populations of adult frogs (Rana pipiens) and toads (Bufo americanus). The activity of frogs and salamanders, as monitored by sand transects, was unchanged following an application of aminocarb at 175 g-AI.ha^{-1} to forest in Quebec, but toads (Bufo americanus) and garter snakes (Thamnophis sirtalis) exhibited delayed declines in activity that may have been caused by reduced

availability of insects as food for the toads (Bider and Bracher 1980). Cholinesterase activity in the brains of green frogs (Rana clamitans melanoto) increased 24 h after treatment of forest in Maine with 168 g-AI.ha^{-1} (Peterson 1976), but the change was not statistically significant.

4.4 EFFECTS ON AQUATIC ECOSYSTEMS

It is the panel's experience that in spite of attempts to leave buffer zones around water bodies, they occasionally are sprayed. It is difficult to shut off aerial emission over short distances when travelling at high speed, and smaller water bodies are not protected except by the filtering action of the forest canopy. Aerial drift may carry insecticide to areas outside the target area and with inadvertent double-swathing and overspraying, the amount reaching a water surface may be more than anticipated. These are, of course, problems peculiar to all aerial spraying, not exclusively to aminocarb.

Residues of aminocarb and adjuvants in water have been documented in Section 2.7. Much of the available information on toxicity of aminocarb to specific organisms is based on laboratory tests where conditions were very different from those in the field. Most laboratory tests were static and concentrations of aminocarb were not permitted to diminish rapidly as occurs in the field. Such tests are useful to determine the relative toxicities of insecticides, but they are only general indicators of what may happen in the field. Natural waters can sometimes be strongly buffered, include various and complex environmental elements, and are subject to natural radiation that affects chemical decomposition; moreover, the concentration of aminocarb diminishes rapidly after a brief introduction and differs greatly over short distances. Also, a dynamic equilibrium may exist between different ecosystem compartments (Section 2.7). For these reasons laboratory tests and field tests directed toward confined organisms are considered separately from field studies where natural waters were contaminated and the effects on wild organisms were monitored.

Most field studies are severely limited by a lack of corollary insecticide residue samples. In much of the literature the evaluations are subjective, sometimes even when data preclude conclusions. The literature on aminocarb has been reviewed (Leonard 1979) but in uncritical fashion. The field monitoring reports are thus reviewed critically in this monograph.

4.4.1 EFFECTS ON FISH

4.4.1.1 Acute Toxicity

The acute toxicities of aminocarb and some of its formulations to fish are tabulated in Table 4-4. Generally, the formulated products

Table 4-4. Acute toxicity of aminocarb and formulations to fish.

Fish Species	Exposure	Test and Response LC_{50} ($mg.L^{-1}$)	References
Rainbow trout fingerlings (*Salmo gairdneri*)	Aminocarb 1.68D oil soluble concentrate containing 18% aminocarb	0.75-0.96, 96 h, static, 15°C	Wells *et al.* (1979)
	Aminocarb (5.4%) formulated with No. 2 and No. 4 fuel oil and emulsifier	3.0, 96 h, static, 15°C	"
"	Nonyl phenol	~ 0.96, 96 h	Environmental Protection Service (1981)
"	1.8F water formulation[b]	21, 96 h, static, 9°C	Szeto and Holmes (1982)
"	1.8F oil formulation[b]	29, 96 h, static, 8°C	"
"	1.8D (19.5% aminocarb, 50.5% nonyl phenol, 30% 585 oil)	0.36, 96 h, static, 8°C	"
Juvenile Atlantic salmon (*Salmo salar*)	Pure aminocarb	8.7, 96 h, static, 10°C	McLeese, *et al.* (1980a)
"	Nonyl phenol	0.9, 96 h, static, 10°C	"
"	Aminocarb (21.7%) formulated with nonyl phenol (51.2%) plus 585 oil	3.5, 96 h, static, 10°C	"
"	Nonyl phenol	0.13-0.19, 96 h, flow-through	McLeese *et al.* (1981)
Bluegill (*Lepomis macrochirus*)	Matacil 1.8-585	0.646, 18°C, static	Nelson and Roney (1978a)
Rainbow trout	Matacil 1.8-585 (19.5% aminocarb, 30% stove oil, 50.1% nonyl phenol)	0.377, 14°C, static	"
"	Matacil technical (95% aminocarb)	8.9, 96 h, static, 14°C, pH 8	Nelson and Roney (1978b)
"	Matacil 1.4 OSC, (17% aminocarb, 35% Panasol AN-3, 48% dodecylphenol)	0.424, 96 h, static, 14°C, pH 8	"
"	"Inert" ingredients in matacil 1.4 OSC (0% aminocarb, 42.2% Panasol AN-3, 57.8% dodecylphenol)	0.418, 96 h, static, 14°C, pH 8	"
"	Matacil 1.8 OSC (18.6% aminocarb, 33.2% Arotex A3470, 48.2% nonyl phenol)	0.3, static, 14°C	Nelson and Roney (1978b)
"	Inert ingredients in Matacil 1.8 OSC (40.8% Arotex A3470, 59.2% nonyl phenol)	0.278, static, 14°C,	"
"	1.8F[a] flowable concentrate	122-175 (trout), 96 h, static	Ernst (1981)
"	1.8F oil formulation	226-350 (trout), 96 h, static	"
"	1.8F water formulation	638-718 (trout), 96 h, static	"
"	Diluent 585 oil	519 (trout), 96 h, static	"
"	Atlox oil	53-748 (trout), 96 h, static	"
"	Sunspray 7-N oil	5600 (trout), 96 h, static	"

Table 4-4. (Cont'd).

Fish Species	Exposure	Test and Response LC_{50} ($mg.L^{-1}$)	References
Channel catfish (Ictalurus punctatus)	Matacil technical (95% aminocarb)	47, 96 h, static, 18-20°C	Nelson and Roney (1978c)
"	Matacil 1.4 OSC (17% aminocarb)	1.4, 96 h, static, 18-20°C	"
"	Inert ingredients in 1.4 OSC	1.5, 96 h, static, 18-20°C	"
"	Matacil 1.8 OSC (18.6% aminocarb	1.1, 96 h, static, 18-20°	"
"	Inert ingredients in 1.8 OSC	1.0, 96 h, static, 18-20°C	"
Rainbow trout and bluegill	Technical aminocarb	5.7 (trout); 5.2 (bluegill)	Lamb and Roney (1975)
"	MAA	0.349 (trout); 0.153 (bluegill)	"
"	FA	15 (trout); 26 (bluegill)	"
"	AA	1.7 (trout); 0.85 (bluegill)	"
"	MFC	>15, 12°C (trout); 23.1, 26°C (bluegill); 96 h; static	Lamb and Roney (1975)
"	Matacil end use dilution (20.5% aminocarb, 50% nonyl phenol, 29.5% 585 oil)	3.5, 15°C (trout); 6.9, 20°C (bluegill); 96-h; static	Nelson and Roney (1979)
Mature bullhead (Ictalurus nebulosus)	Matacil technical	≥63, 96 h, static	Qadri and Richardson (1980)
Immature bullhead	"	100, 96 h, continuous-flow	"
Silvery minnow (Hybognathus nuchalis)	"	34, 96 h, static	"
Cutthroat trout (Salmo clarki)	Matacil technical	28	Woodward and Mauck (1980)
"	17% formulation	0.52 (cited as 0.088 $mg\text{-}AI.L^{-1}$)	"

[α] Aminocarb suspended in sunspray oil with 3% other ingredients.

[β] 33% 1.8F flowable concentrate[α] with Atlox 3409F (1.25%) and water or with diluent 585.

are more toxic than technical aminocarb. For example, Nelson and Roney (1978a,b) reported the LC_{50} of technical aminocarb (95% aminocarb) to rainbow trout as 8.9 $mg.L^{-1}$, compared with LC_{50} values of 0.4 and 0.3 $mg.L^{-1}$ for two "oil-soluble concentrates" containing 17 and 18.6% aminocarb respectively. Nelson and Roney (1978b) reported tests with the "inert ingredients" in two formulations of aminocarb: one contained 42.4% Panasol AN-3 and 57.8% of dodecylphenol, and had an LC_{50} of 0.4 $mg.L^{-1}$ to fish; the other contained 40.8% Arotex A3470 and 59.2% nonyl phenol, and had an LC_{50} of 0.28 $mg.L^{-1}$. Similar results have been obtained with other organisms (Table 4-4). Clearly, much of the toxicity to fish of aminocarb formulations currently in use can be attributed to formulation components other than aminocarb itself.

On the basis of preliminary data (Ernst 1981), the 1.8F concentrate (not registered for operational use) is considerably less toxic to rainbow trout than is the 1.8D concentrate. The toxicity of the 1.8F water formulation appears to be due entirely to its aminocarb content. The 1.8F formulations do not contain nonyl phenol.

There is at least one potential metabolic product of aminocarb that is substantially more toxic to fish than the parent compound. The LC_{50} of MAA[α] to trout is 0.349 $mg.L^{-1}$ compared with 5.7 $mg.L^{-1}$ for aminocarb (Lamb and Roney 1975).

4.4.1.2 Field Monitoring

Current residues measured in streams and lakes (Section 2.7) are well below those required to produce fish kills (Table 2-7), and indeed fish kills have not, so far, been reported with aminocarb spraying in Canada (Coady 1978; Kingsbury 1978; Holmes 1979).

Sublethal responses have been observed, however, using analyses of fish stomach contents and enzyme (cholinesterase) activity. Holmes (1979) found that brook trout (Salvelinus fontinalis) fed opportunistically on terrestrial insects knocked down by aminocarb spraying in Quebec. Slimy sculpins (Cottus cognatus) did not take advantage of the terrestrial insects, but did shift feeding from baetid mayfly nymphs to other insects, notably burrowing mayfly nymphs and larvae of crane flies, blackflies, and chironomids. Similarly, blacknose dace (Rhinichthys atratulus) changed from feeding on heptagenid mayfly nymphs, stonefly nymphs and caddis fly larvae to blackfly larvae, chironomid larvae and terrestrial lepidoptera larvae.

Brown (1978) assayed brook trout brain cholinesterase activity from fish in spray zones in Maine. In one stream the enzyme activity dropped by about 20% on the day after spraying and returned to prespray levels 2 d later. In the second stream, however, enzyme activity apparently increased after spraying and remained at the elevated levels

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[α] See inside back cover.

throughout the 30-d sampling period. No explanation for the elevation in enzyme activity was offered. The depression after treatment in the first stream was not statistically significant. No dead or weakened fish were reported from studies with caged fish for catches from barrier nets. An earlier study (Marancik 1976) reported large depressions in cholinesterase activity in brook trout (25 and 95% depression after 24 and 48 h respectively) with recovery to normal levels in 144 h. In spite of these cholinesterase effects, the fish "did not appear to be distressed in any way".

4.4.1.3 Residue Dynamics

Analyses of fish following spraying have consistently shown little or no accumulation of aminocarb in whole body fish tissue. Marancik (1976) reported whole body residues up to 0.2 $\mu g.g^{-1}$ in brook trout and white suckers (Catostomus commersoni) following forest spraying in Maine. Holmes (1979) found no residues above detection limits of 0.003 $\mu g.g^{-1}$ in any fish examined from Quebec spray zones. Earlier, a case of fish poisoning had been suspected but no residues of aminocarb were found (Sundaram 1976). Coady (1978) found that two of twenty-six fish examined after spraying in Newfoundland contained aminocarb at concentrations of 0.02 and 0.04 $\mu g.g^{-1}$.

Aminocarb would not be expected to accumulate efficiently in fish. Log K_{ow} has been calculated as 2.91, predicted as 1.6 and measured as 1.85 (Section 2.1.1). Neely et al. (1974) derived the following expressions to predict bioconcentration factors (BCF):

$$\log BCF = 0.542 \log K_{ow} + 0.124 \qquad (4\text{-}1)$$

Using this expression, the anticipated bioaccumulation at steady state is only 10 to 50-fold above the concentration in the water. Chiou et al. (1977) have derived a similar expression using water solubility instead of the partition coefficient:

$$\log BCF = 3.41 - 0.508 \log S\ (\mu mol.L^{-1}) \qquad (4\text{-}2)$$

This equation indicates a BCF of about 80-fold (using S = 2000 $mg.L^{-1}$). Field observations suggest even lower BCFs, but the rapid dissipation of aminocarb from natural spray zones makes any calculation uncertain since fish almost certainly would not reach the maximum steady state BCF predicted on the basis of these relations.

Lamb and Roney (1976) assayed the accumulation of radioactivity in channel catfish (Ictalurus punctatus) following exposure to ring-labelled ^{14}C-aminocarb (Figure 4-1). These uptake data indicate BCFs smaller than 10, and clearance data for total radioactivity indicate a $t_{\frac{1}{2}}$ less than or equal to 10 d. The regression equation for depuration of the label was:

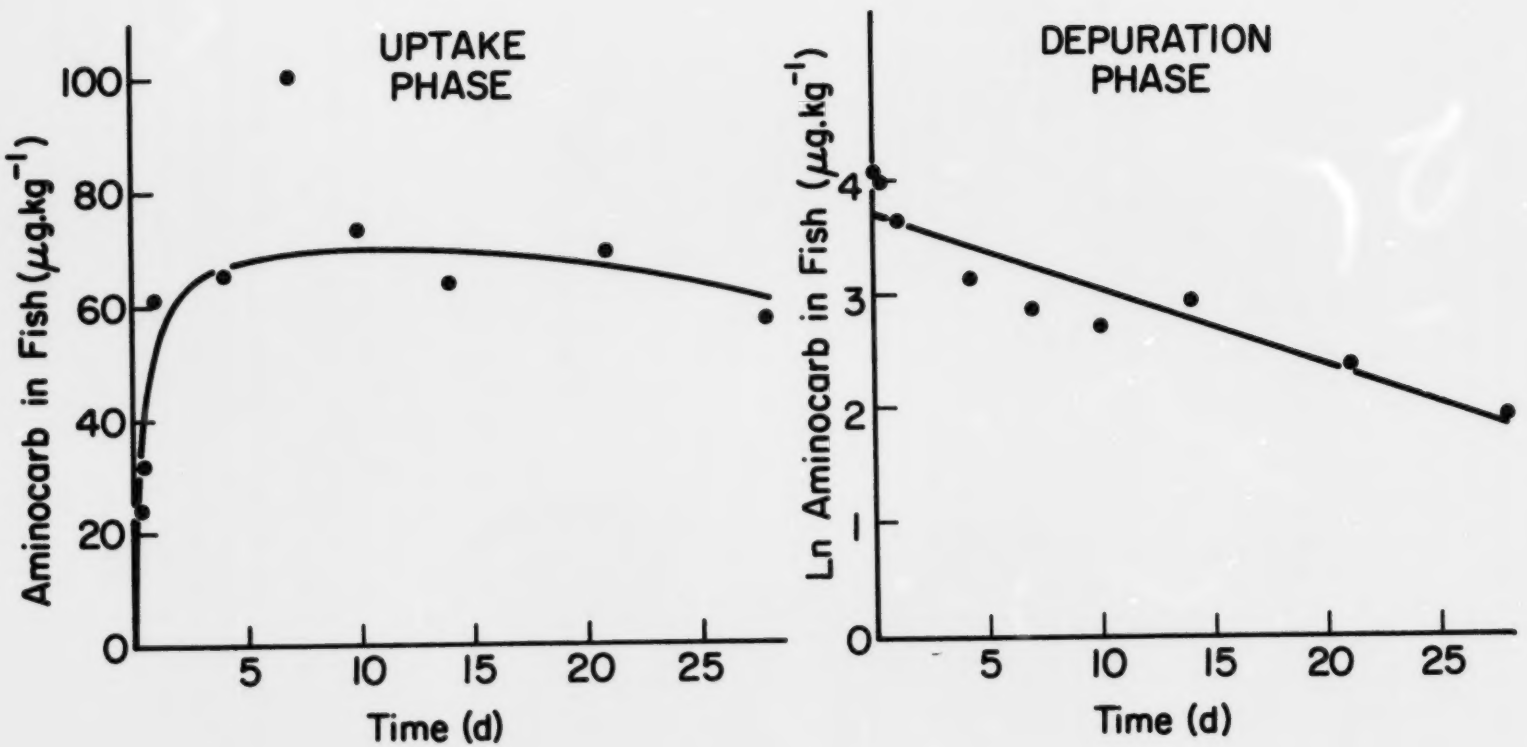

Figure 4-1. Uptake and depuration of ^{14}C-aminocarb by channel catfish exposed to 10 $\mu g.L^{-1}$ in flowing water at 27°C for 28 d (uptake phase) and then maintained in water free of aminocarb for a further 28 d (depuration phase). Data plotted from those of Lamb and Roney (1976). These data could also be plotted as a 2-phase process.

$\log_e Y = -0.0659 X + 3.6953$

where Y = radioactivity remaining in fish, as aminocarb, in $\mu g.kg^{-1}$

and X = duration of depuration period in days

$r = -0.9258$, $df = 7$

The actual $t_{\frac{1}{2}}$ of intact aminocarb would be somewhat less than 10 d because the radioactivity measurement would not discriminate among aminocarb and potential ^{14}C-products formed from it. Lamb and Roney (1976) noted that solvent recoverable residues at the end of the 28-d exposure period were 22% extractable into hexane and 78% extractable into acetonitrile.

4.4.1.4 Distribution in Fish Tissues

Lamb and Roney (1976) exposed channel catfish to ^{14}C-aminocarb for 28 d, then divided them into two composite samples, one comprising head, viscera and scales and the other comprised edible tissue. The former sample contained 71% of body weight and 75% of solvent recoverable residue (21% into hexane and 54% into acetonitrile). The latter sample contained 29% of body weight and 25% of recoverable residues (only 1% extractable into hexane and 24% into acetonitrile). Qadri and Richardson (1980), in a preliminary report, gave distribution data based on radioactivity content in tissues of bullhead (Ictalurus nebulosus) exposed to ^{14}C-aminocarb at 41 $mg.L^{-1}$, for 96 h at 18°C (Table 4-5). These results indicated that major internal organs, constituting only 12.5% of body weight, contained over 50% of the aminocarb label. Fat contained the highest concentration of label, although it contributed only a minor proportion of body weight. This study did not discriminate between aminocarb and metabolites.

4.4.1.5 Cholinesterase Inhibition

Abou-Donia and Menzel (1967) reported 50% fish brain cholinesterase inhibition (I_{50}) at 3.9×10^{-6} M. Heyndricks and Von Hoof (1971) reported the I_{50} for horse plasma cholinesterase at 3.8×10^{-5} M. Guilbault et al. (1972) found an I_{50} value of 5×10^{-5} M using lake trout (Salvelinus namaycush) brain as the enzyme source. The highest concentrations of aminocarb measured in fish following an application of 169 $g.ha^{-1}$ in Maine were 0.2 $\mu g.g^{-1}$ in brook trout and white suckers (Marancik 1976). The lower value for cholinesterase inhibitors (812 $\mu g.L^{-1}$) exceeds these concentrations by about 4-fold. If in vitro inhibition studies provide a reasonable estimate of concentrations required to produce inhibition in vivo, then aminocarb would have to concentrate selectively in brain by at least several-fold over whole body residues in order to seriously inhibit fish brain cholinesterase. The distribution data (Table 4-5) indicate residues in brain to be

Table 4-5. Distribution of aminocarb (based on radioactivity) in body organs of brown bullhead exposed to ^{14}C-aminocarb at 18°C for 96 h at 41 $mg.L^{-1}$ (Qadri and Richardson 1980).

Organ of bullhead	Aminocarb in organ ($\mu g.g^{-1}$ wet)	Percent of total body burden in organ
skin	128	12.4
stomach and intestine	317	15.4
kidney	198	6.1
liver	250	11.4
fat	460	3.9
brain	156	3.5
heart	271	1.6
carcass	37	46.2

approximately 4-fold higher than those in "carcass". Thus, the study in which brook trout from a sprayed stream were found to have reduced brain cholinesterase activities (Marancik 1976) appears to be consistent with the *in vitro* inhibition studies, and with the residues observed on the fish.

4.4.1.6 Nonyl Phenol Effects

It is clear from results presented in Table 4-4 that much of the fish toxicity associated with current operational aminocarb formulations is due to formulation components other than aminocarb itself. McLeese *et al.* (1981) (Table 4-4) found that nonyl phenol was toxic to juvenile Atlantic salmon at 0.13 $mg.L^{-1}$, and so the concentrations of up to 1.1 $mg.L^{-1}$ reported for an Ontario field site with standing water (Section 2.7.2) clearly reached toxic nonyl phenol concentrations. Fish sampled from the Ontario field site contained no measurable nonyl phenol (Holmes and Kingsbury 1980). Cage bioassays were inconclusive. Some brook trout caged in the treatment zone died in unexpectedly high numbers starting about 5 d after treatment, but this was thought to be related to factors other than the treatment since it was not found with 35 d bioassays with lake trout exposed to nonyl phenol in concentrations up to 40 $\mu g.L^{-1}$.

Nonyl phenol has a log K_{ow} of 4.2 (McLeese *et al.* 1981). Using the relation of Neely *et al.* (1974):

$$\log BCF = 0.542 \log K_{ow} + 0.124 \qquad (4\text{-}4)$$

the BCF predicted in fish is 252. McLeese *et al.* (1981) report a measured BCF of 280 in salmon; the BCF appeared to decrease over the 4 d of their experiment.

The toxicity of nonyl phenol to rainbow trout (*Salmo gairdneri*) eggs was measured (Environmental Protection Service 1981). These data (Table 4-6) show that the 24-h LC_{50} is less than 1 $mg.L^{-1}$.

4.4.2 TOXICITY TO AQUATIC ORGANISMS OTHER THAN FISH

The toxicity of aminocarb and adjuvants to a wide range of aquatic organisms has been determined. Much of this information is difficult to interpret because the nature of the formulation used is often not specifically stated. Solvents added to technical aminocarb are not always specified. Also, while toxicities are usually expressed in terms of aminocarb concentrations, some authors report the toxicity of the formulation. The difference is not always clearly specified. The same problems apply to the field data. In Tables 4-7 and 4-8 the chemical tested is described using chemical common names whenever possible, and concentrations given as $weight.volume^{-1}$. It should be

Table 4-6. Toxicity (% mortality)[α] of nonyl phenol to Salmo gairdneri eggs (exposure 24 h, static, aerated). Data in brackets have been corrected using Abbott's formula and mean of two controls.

Nonyl phenol ($\mu g.L^{-1}$)	Recovery time (d) 0	1	2	4
Control	0	0	1.5	50
Alcohol[β]	0	0	2.0	48
100	0	16.5	21.5(20.0)	54.5(10.8)
320	0	0	4.5(2.7)	55.0(11.8)
1000	4.0	9.5	93.0(92.9)	98.5(97.1)
3200	7.5	13.0	82.5(82.2)	93.0(86.3)
10000	100	100	100(100)	100(100)

[α] Some eggs died before hatch, some as hatchlings; > 100 eggs/tank.

[β] Clean water + ethanol at highest concentrations found in treatment.

Table 4-7. Toxicity of aminocarb, aminocarb formulation, and formulation components to aquatic and soil bacteria, and aquatic fungi, algae, and higher plants. All tests under static conditions unless stated otherwise.

Organism		Chemical	Dose	Response	Reference
Bacillus subtilus	Bacterium	Aminocarb, analytical standard	2 to 10,000 mg.L^{-1}, 24 h	No growth inhibition	Strankowski and Minor (1978)
Cellulomonas flavigens	"	"	"	"	"
Pseudomonas aeruginosa	"	"	"	"	"
Streptomyces scabies	"	"	"	"	"
Aspergillus niger	Fungus	"	2 to 10 mg.L^{-1}, 24-48 h	2 to 10% growth inhibition	"
Trichoderma viride	"	"	"	"	"
Phycomyces nitens	"	"	"	"	
Penicillium daleae	"	"	Up to 10 mg.L^{-1}, 24-48 h	No growth inhibition	"
Aquatic Hyphomycetes	Fungi	Aminocarb formulation in fuel oil	Up to 90 µg-AI.L^{-1}, 60 d, agitated	Sporulation, germination and growth occurred	Eidt et al. (1979)
Decomposition microorganisms	"	Aminocarb formulation in 585	100 µg-AI.L^{-1}, 24 h, agitated	O_2 consumption increased	Ahern (1980)
Dunaliella euchlora	Unicellular alga	Bayer 44646	1 mg.L^{-1}, 4 h	9.1% decrease in productivity	Mobay (undated)
Platymonas sp.	"	"	"	25.4% decrease in productivity	"
Selanastrum capricornutum	Green alga	Aminocarb (99.3%)	0.1 mg.L^{-1}, 14 d	LC_{50}	Couture et al. (1979)
"	"	Aminocarb formulation (17% AI)	0.1 mg-AI.L^{-1}, 14 d	LC_{50}	"
"	"	Aminocarb formulation in 585 (6.3% AI)	<0.1 mg-AI.L^{-1}, 14 d	LC_{50}	"
Chlamydomonas variabilis	Natural phytoplankton	Aminocarb (99.3% aminocarb)	0.8 mg.L^{-1}, 24 h	LC_{50}	"
"	"	Aminocarb formulation (17% AI)	0.6 mg-AI.L^{-1}, 24 h	LC_{50}	"
"	"	Aminocarb formulation in 585 (6.3% AI)	0.1 mg-AI.L^{-1}, 24 h	LC_{50}	"
"	"	Bayer 44646	1 mg.L^{-1}, 4 h	No effect	Mobay (undated)
Lemna minor	Duckweed	Nonyl phenol	0.5 mg.L^{-1}, 4 d	Stopped growth	Prasad (1981)
"	"	"	0.250 mg.L^{-1} renewed daily, 4 d	Stopped growth	"
Salvinia molesta	"	"	2.5 mg.L^{-1} and higher, 9 d	Stopped growth	"
Lemna minor	"	Aminocarb	~10 mg.L^{-1}	Phytotoxicity and growth inhibition or no effect	"

Table 4-8. Toxicity of aminocarb formulation, and formulation components to aquatic animals other than fish. All tests were static unless otherwise specified.

Organism		Chemical	Dose	Response	Reference
Nereis virens	Marine annelid	585 solvent oil	5.0 mg.L^{-1}, 96 h	LC_{50}	McLeese *et al.* (1980b)
Anodonta cataractae	Freshwater clam	Aminocarb	>5.0 mg.L^{-1}, 144 h	LC_{50}	"
"	"	Nonyl phenol	5.0 mg.L^{-1}, 144 h	LC_{50}	"
"	"	585 solvent oil	>5.0 mg.L^{-1}, 144 h	LC_{50}	"
"	"	Aminocarb formulation	>1.0 mg.L^{-1}, 144 h	LC_{50}	"
Anodonta sp.	"	1.8F water formulation (5.1% AI)	260 mg.L^{-1}; 96 h	LC_{50}	Ernst (1981)
"	"	1.8F 585 oil formulation (5.3% AI)	260 mg.L^{-1}; 96 h	LC_{50}	"
"	"	1.8F 585 oil formulation (53% AI)	1800 mg.L^{-1}; 96 h	LC_{50}	"
Mya arenaria	Soft-shelled clam	Nonyl phenol	>1.0 mg.L^{-1}, 360 h	LC_{50}	"
"	"	585 solvent oil	>5.0 mg.L^{-1}, 144 h	LC_{50}	"
Crassostrea virginica	Oyster	Bayer 44646	1 mg.L^{-1}, 96 h	50% decrease in shell growth	Butler (1962)
Mytilus edulis	Mussel	Aminocarb	25-402 µg.L^{-1}, 4 d	Peak conc. in tissue at 2 d	McLeese *et al.* (1980a)
"	"	Nonyl phenol	0.1-1.13 mg.L^{-1}, 4 d	Peak conc. in tissue at 2 d	"
"	"	585 solvent	0.396 mg.L^{-1}, 2.5 d	Peak conc. in tissue at 2 d	"
"	"	1.8F water formulation (5.1% AI)	1000 mg.L^{-1}; 96 h	LC_{50}	Ernst (1981)
"	"	1.8F-585 oil formulation (5.3% AI)	1000 mg.L^{-1}; 96 h	LC_{50}	"
"	"	1.8F 585 oil formulation (5.3% AI)	1079 mg.L^{-1}; 96 h	LC_{50}	"
Species not stated	Starfish	Aminocarb	10 mg.L^{-1}	No effect	Mackenzie (1962)
"	"	"	100 mg.L^{-1}	Lethal	"
Gammarus pseudolimnaeus	Scud	Aminocarb	12 (8-18) µg.L^{-1}, 96 h	LC_{50} (95% CI)	Schoettger and Mauck (1978)
"	"	Aminocarb (98%)	2.2 (1.5-3.3) mg.L^{-1}, 96 h, pH 7.5	LC_{50} (95% CI)	Woodward and Mauck (1980)
"	"	Aminocarb (98%)	1.0 mg.L^{-1}, 96 h, pH 8.5	LC_{50}	"
Gammarus lacustrus	Scud	Aminocarb	39(30-51) mg.L^{-1}, 24 h 29(21-39) mg.L^{-1}, 48 h 12(8-17) mg.L^{-1}, 96 h	LC_{50} LC_{50} LC_{50}	Sanders (1969)
Daphnia magna	Water flea	Aminocarb	19 (11-32) µg.L^{-1}, 48 h	LC_{50} (95% CI)	Nelson (1978a)
"	"	Aminocarb formulation in 585 (19.9% AI)	22 (11-43) µg-AI.L^{-1}, 48 h	LC_{50} (95% CI)	Nelson (1978b)
"	"	Aminocarb 99.3%	0.2 µg.L^{-1}, 24 h	LC_{50}	Couture *et al.* (1979)
"	"	Aminocarb formulation (17% AI)	0.4 mg-AI.L^{-1}, 24 h	LC_{50}	"
"	"	Aminocarb formulation in 585 (6.3% AI)	<0.1 mg-AI.L^{-1}, 24 h	LC_{50}	"

Table 4-8. (Cont'd).

Organism		Chemical	Dose	Response	Reference
Daphnia pulex	Water flea	1.0F water formulation (5.1% AI)	1.1 (0.3-3.2) mg.L^{-1}, 48 h	LC_{50} (95% CI)	Ernst (1981)
"	"	1.0F 585 oil formulation (5.3% AI)	0.4 (0.1-1.0) mg.L^{-1}, 48 h	LC_{50} (95% CI)	"
"	"	Nonyl phenol	140(79-201), 176 (114-238), 190 mL.L^{-1}, 48 h	LC_{50}'s in 3 tests	Environmental Protection Service (1981)
Species not stated	Fiddler crab	Aminocarb	1.1 x 10^{-2} M	I_{50} (50% AChE inhibition)	Guilbault et al. (1972)
"	"	"	4.5 x 10^{-5} M	I_{10} (10% AChE inhibition)	"
"	Crayfish	"	1.0 x 10^{-2} M	I_{50} (50% AChE inhibition)	"
"	"	"	1.6 x 10^{-5} M	I_{10} (10% AChE inhibition)	"
Orconectes limosus	"	Aminocarb in ethanol	32.7 (23.5-40.1) mg.L^{-1}, renewed daily, 96 h	LC_{50} (95% CI)	Sundaram and Szeto (1979)
Crangon septemspinosa	Marine shrimp	Aminocarb	0.2 mg.L^{-1}, 96 h	LC_{50}	McLeese et al. (1980b)
"	"	Nonyl phenol	0.4 mg.L^{-1}, 96 h	LC_{50}	"
"	"	" "	0.3 mg.L^{-1}, 96 h	LC_{50}	McLeese et al. (1981)
"	"	585 solvent oil	5.0 mg.L^{-1}, 96 h	LC_{50}	McLeese et al. (1980b)
"	"	Aminocarb formulation	0.55 mg.L^{-1}, 96 h	LC_{50}	"
Pandalus montagui	Pink shrimp	585 solvent oil	0.2 mg.L^{-1}, 96 h	LC_{50}	"
Penaeus aztecus	Brown shrimp	Bayer 44646	0.32 mg.L^{-1}, 24 h and 48 h	LC_{50} mortality or paralysis	Lowe (1962)
Homarus americanus	Lobster	Nonyl phenol	0.2 mg.L^{-1}, 96 h	LC_{50}	McLeese et al. (1980b)
Pteronarcella badia	Stonefly	Aminocarb (98%)	28(18-43) µg.L^{-1}, 96 h, pH 6.5	LC_{50} (95% CI)	Woodward and Mauck (1980)
"	"	"	19(15-26) µg.L^{-1}, 96 h, pH 7.5	LC_{50} (95% CI)	"
"	"	"	26(20-33) µg.L^{-1}, 96 h, pH 8.5	LC_{50} (95% CI)	"
Chironomus riparius	Midge	Aminocarb	376.6 (329.7-428.5), 24 h	LC_{50} (95% CI)	Estenik and Collins (1979)
Rana clamitans melanota	Green tree frog	Aminocarb aerial spray	168 g-AI.ha^{-1}	Slight increase in AChE activity	Peterson (1976)
Rana clamitans tadpoles	Green frog	Aminocarb 75% wettable powder	247 mg.L^{-1}, 24 h	LC_{50}	Lyons et al. (1976)

[α] Aminocarb suspended in sunspray 7N oil with 3% other ingredients.

[F] "Blended" tests were run by homogenizing stock toxicant in a blender prior to introduction to exposure chambers.

[Y] CI = confidence interval.

noted that aminocarb formulations, expressed as lethality of aminocarb, are generally more toxic than is technical aminocarb (McLeese et al. 1980b). The exception may be the 1.8F water formulation and concentrate (not in operational use), which is reported to be less toxic to several organisms (Table 4-7) (Ernst 1981).

4.4.2.1 Bacteria and Fungi

With four species of soil bacteria, Strankowski and Minor (1978) could not measure growth inhibition at aminocarb concentrations up to 10 $g.L^{-1}$, over a million times that resulting from forest spraying at 70 $g\text{-}AI.ha^{-1}$. They demonstrated some growth inhibition of two species of soil Actinomycetes (Trichoderma viride and Phycomyces nitens) in pure culture at 2 $mg.L^{-1}$, inhibition of a third species (Aspergillus niger) at 10 mg.L, and inhibition of a fourth species (Penicillium daleae) at 100 $mg.L^{-1}$. These tests involved incubating two replicate discs from pure cultures for 24-48 h on agar containing the test chemical and comparing growth with a control.

Eidt et al. (1979, 1980) and Eidt (1980b) did not obtain consistent data on respiration and decomposition of leaf tissue by aquatic Hyphomycetes. At starting concentration of 90 $\mu g.L^{-1}$ of aminocarb, they observed sporulation, germination of spores, and growth of several species in agitated flasks of spiked water even after 60 d. It was not noted in the report, but the aminocarb was in a standard formulation containing nonyl phenol and fuel oil.

In a field experiment, Ahern (1980) treated a stream with aminocarb formulation (100 $\mu g\text{-}AI.L^{-1}$) for 24 h. He found that after removal to the laboratory, the microorganisms on streamside litter, that had been immersed in the treated stream, consumed significantly more oxygen than those on litter immersed above the treated stretch.

4.4.2.2 Algae

Two tests in the 1960's (Mobay Chemical Corporation, undated) indicated a 9.1% decrease in productivity of Dunaliella euchlora and 25.4% decrease in productivity of Platymonas sp. cultured for 4 h in medium containing 1 $mg.L^{-1}$ of Bayer 44646 (probably technical aminocarb dissolved in a solvent such as ethanol). The same concentration had no effect on a natural plankton community.

Couture et al. (1979) determined the 14-d LC_{50} for Selanastrum capricornutum and the 24-h LC_{50} for Chlamydomonas variabilis using technical aminocarb, a formulation containing 165 $g\text{-}AI.L^{-1}$ plus nonyl phenol and 585 oil, and 585 solvent oil. Their LC_{50}'s are tabulated (Table 4-9) and presumably were measured as weight per volume. The toxicity of formulation to C. variabilis is greater than that of

Table 4-9. Toxicity of aminocarb to Selanastrum capricornutum (14-d LC_{50}) and Chlamydomonas variabilis (24-h LC_{50}).

Ingredient	14-d LC_{50} ($mg.L^{-1}$) S. capricornutum		C. variabilis	
	formulation	AI	formulation	AI
aminocarb (99.3% AI)	0.1	0.1	0.8	0.8
aminocarb formulation (17% AI)	0.8	0.1	3.5	0.6
aminocarb formulation in 585 oil (6.3% AI)	1.0	0.1	< 6.5	< 0.1
585 solvent oil	2.4	-	72.0	-

aminocarb alone, indicating that nonyl phenol may be more toxic than aminocarb.

Elner et al. (1982) reported a 50% decrease in carbon assimilation by natural algal communities exposed to aminocarb (formulated with nonyl phenol and 585 oil) at 0.9 mg-AI.L^{-1}. A concentration of 1.5 mg-AI.L^{-1} inhibited all detectable carbon uptake. Algal production was reported to recover within 72 h at concentrations up to 2.2 mg-AI.L^{-1}. The authors point out that their experiments do not differentiate between the effects of nonyl phenol and aminocarb.

Weinberger and Rea (1981) reported that nonyl phenol, at approximately 1 mg.L^{-1} for 1 h caused 90% mortality of flagellated algae in laboratory microcosms. The survivors reproduced to pretreatment populations within 28 d. The significance of these studies has not been confirmed under less confined conditions.

4.4.2.3 Vascular Plants

Prasad (1981) found that aminocarb (10 mg.L^{-1}) "either had no effect or caused phytotoxicity" to the duckweed, Lemna minor. He found that ^{14}C-aminocarb was absorbed rapidly, accumulated several-fold, and metabolized into several compounds with various retention characteristics on a thin layer chromatogram. These treatments presumably did not include nonyl phenol for which separate tests were run. He treated cultures of the duckweed Lemna minor and Salvinia molesta with nonyl phenol at 0, and eight concentrations from 0.125 to 25 mg.L^{-1}. When he renewed the solution daily, growth of L. minor was stopped in 0.25 mg.L^{-1} and higher concentrations. When the solution was not renewed daily, growth was not stopped but slowed at 0.500 mg.L^{-1}, the highest concentration used. S. molesta growth was stopped at concentrations of 2.5 mg.L^{-1} and higher. He suggested that the mode of action was disruption of the membrane integrity of organelles.

Prasad (undated) reported bioassay results with duckweed (Lemna minor) and Salvinia molesta exposed to nonyl phenol. Both plants showed dose-dependent growth responses over concentrations ranging upward from 125 µg.L^{-1}.

As stated in Chapter 2, it appears likely that phytotoxic concentrations of nonyl phenol might be expected in shallow standing water following spraying.

Aminocarb is accumulated from water by aquatic macrophytes. Weinberger and Ouellette (1981) reported that submerged hornworts (Ceratophyllum demersum) accumulated aminocarb to levels of 1200 µg.g^{-1} and 600 mg.g^{-1} in 20 d exposures (at 10 mg.L^{-1}) under light and dark conditions respectively. Plants killed by freezing accumulated less than 100 µg.g^{-1} under the same conditions. The presence of formulation

adjuvants had little or no effect on the accumulation of aminocarb, although they were toxic to the plants. Analysis of plant extracts indicated that most labelled material in the plants was underivatized aminocarb.

4.4.2.4 Annelida

The marine worm, Nereis virens, has a high tolerance to 585 solvent oil; McLeese et al. (1980b) reported a 96-h LC_{50} of 5.0 $mg.L^{-1}$ for 585 oil. They did not test aminocarb or nonyl phenol on this animal.

4.4.2.5 Mollusca

Early studies (Butler 1962) with Bayer 44646 described a 50% decrease in shell growth of the oyster Crassostrea virginica at 1 $mg.L^{-1}$ for 96 h. Several other references to toxicity to oysters in other Mobay Chemical Corporation reports are based on the same data.

McLeese (1980) and McLeese et al. (1980b) studied the uptake of components of the aminocarb formulation by the mussel Mytilus edulis, in static tests. They found that in aminocarb at 0.025-0.402 $mg.L^{-1}$ for 4 d, the concentration in tissue peaked at 2 d and none was detected 1 d after exposure ceased. In nonyl phenol, at 0.1-1.13 $mg.L^{-1}$ for 4 d, the concentration peaked in 2 d, and some remained 1 d after exposure ceased. The kinetic accumulation coefficient (the ratio of uptake to excretion rate constants) was 10. Comparable effects for 585 solvent oil, at 0.396 $mg.L^{-1}$ for 2.5 d, were obtained, but the concentration in tissue returned to baseline levels in 12 h. The authors concluded that aminocarb and nonyl phenol, at concentrations of 0.01 $mg.L^{-1}$, are not likely to result in significant contamination of bivalves. The 585 oil disappeared rapidly in seawater and significant accumulation by bivalves seemed unlikely. Tests are presently underway to determine if filter feeding bivalves concentrate particulate aminocarb (1.8F formulation) to a greater extent than soluble aminocarb.

The 360-h LC_{50} of the soft-shelled clam Mya arenaria for nonyl phenol is 1.0 $mg.L^{-1}$ and for 585 solvent oil, 5.0 $mg.L^{-1}$ (McLeese et al. 1980b). Aminocarb and the field mixture were not tested on M. arenaria. However, the toxicity of all fractions and the aminocarb formulations were determined for the freshwater clam Anodonta cataractae (McLeese et al. 1980b). The 96-h LC_{50} for nonyl phenol was 5.0 $mg.L^{-1}$ and for aminocarb, 585 solvent oil, and the formulation it was >5.0 $mg.L^{-1}$, the highest concentrations tested.

A histopathologic study (Li 1981) showed that when shellfish are exposed to high concentrations of formulated aminocarb, gill tissues are affected most. The effect is manifested by separation of gill filaments and development of edema.

4.4.2.6 Echinodermata

Mackenzie (1962) exposed an unspecified starfish species to concentrations of 10 $mg.L^{-1}$ and 100 $mg.L^{-1}$ technical aminocarb. The higher concentration was lethal, and the lower concentration had no effect, but the duration of exposure was not stated.

4.4.2.7 Crustacea

In the earliest work with crustaceans, Sanders (1969) found a 96-h LC_{50} of 12 $\mu g.L^{-1}$ for Gammarus lacustrus, probably using technical aminocarb dissolved in alcohol. He also determined the 24-h LC_{50} as 39 $\mu g.L^{-1}$, and the 48-h LC_{50} as 29 $\mu g.L^{-1}$. Similarly, Schoettger and Mauck (1978) determined the 96-h LC_{50} for Gammarus pseudolimnaeus to be 12 $\mu g.L^{-1}$. It is difficult to tell whether they used technical aminocarb or the aminocarb field formulation, which would have contained an alkyl phenol and fuel oil or 585 solvent oil. Woodward and Mauck (1980), using 98% aminocarb, got a 96-h LC_{50} of 2.2 $mg.L^{-1}$ at pH 7.5. This suggests that Schoettger and Mauck had used the field formulation because they had found it more toxic to brook trout than the technical aminocarb. However, they stated that they diluted the insecticide formulations they tested with distilled water, which, with the oil-based aminocarb field formulation, is not possible.

The water flea Daphnia magna has a sensitivity to aminocarb similar to that of Gammarus. The 48-h LC_{50} for technical aminocarb is 19 $\mu g.L^{-1}$ (Nelson 1978a) and for aminocarb formulated in 585 oil (199 g aminocarb.L^{-1}) is 22 $\mu g.L^{-1}$ (presumably AI) (Nelson 1978b). The toxicity curves are presented in Figure 4-2. Nelson's test solution for technical aminocarb was 10 mg aminocarb in 5 mL acetone in 100 mL distilled water added to the hard water medium. The aminocarb formulation in 585 oil was added to a similar aqueous medium but it is not clear how Nelson mixed the oil and water. In view of these results, it is surprising that Couture et al. (1979) determined the 24-h LC_{50} to be 100 $\mu g.L^{-1}$ AI using aminocarb formulation (168 g-AI.L^{-1}, diluted in 585 at the ratio of 37.2:62.8) and 0.2 $\mu g.L^{-1}$ using technical aminocarb. Expressed as toxicity of the formulation, on the other hand, the toxicity was 3200 $\mu g.L^{-1}$. The 24-h LC_{50}'s determined by Couture et al. (1979) for Daphnia magna are listed in Table 4-10. Figure 4-3 shows the toxicity curve of nonyl phenol to Daphnia pulex (Environmental Protection Service 1981).

Couture et al. (1979) also found, in separate experiments, that the toxicity of aminocarb formulation diminished as the temperature rose from 5 to 20°C and as the pH increased from 6.2 to 7.9. They investigated the effects of nitrogen and phosphorus concentration, but got inconclusive results. The formulations used by Nelson (1978b) and by Couture probably contained an alkyl phenol as a primary solvent.

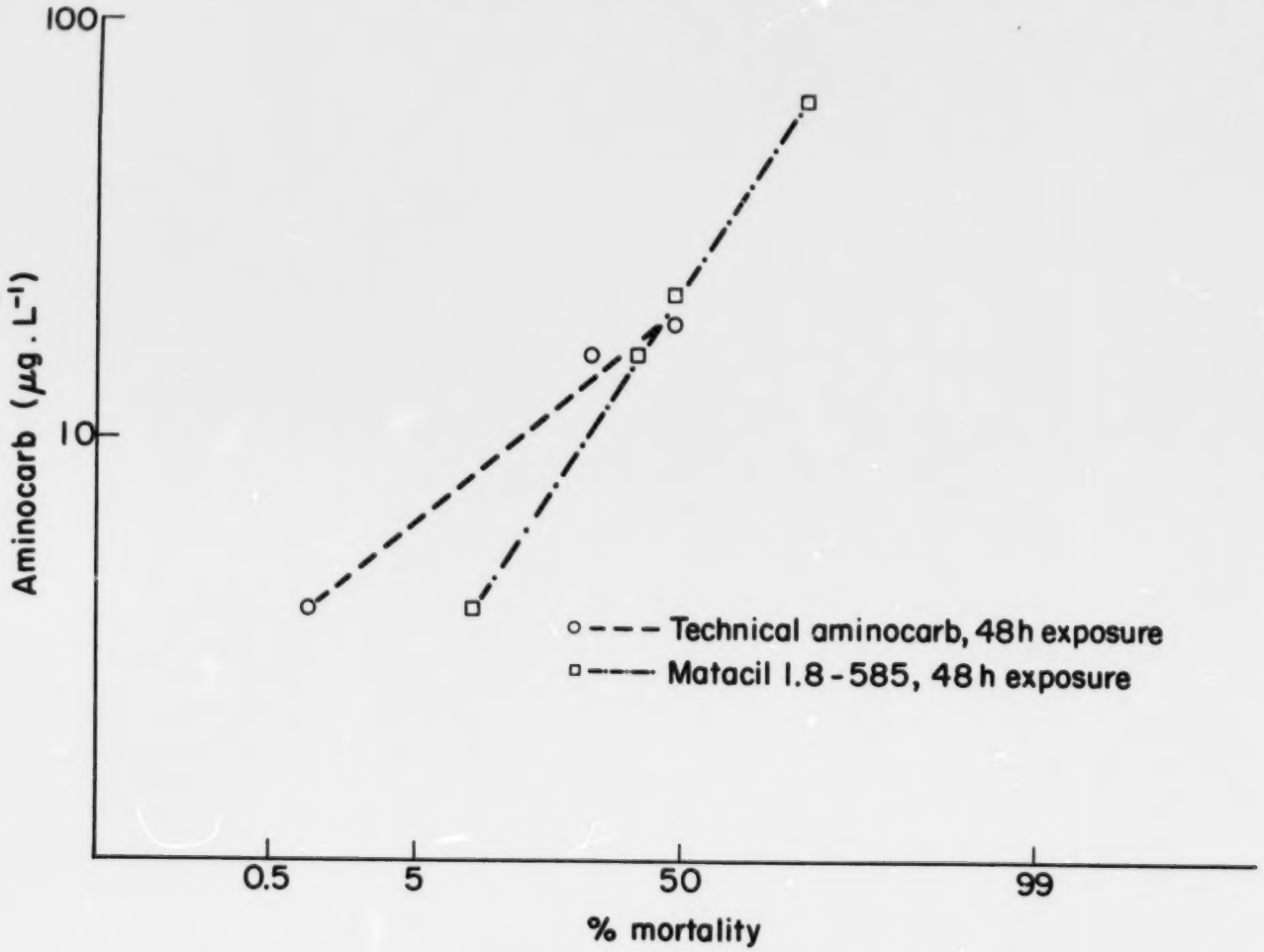

Figure 4-2. Toxicity of aminocarb and formulation to Daphnia magna (after Nelson et al. 1978a,b).

Table 4-10. 24-h LC_{50} of aminocarb and formulation for Daphnia magna.

Ingredient	24-h LC_{50} ($\mu g.L^{-1}$)	
	formulation	active ingredient
Aminocarb 99.3%	-	0.2
Aminocarb formulation (168 g-AI.L^{-1})	2100	400
Aminocarb formulation in 585 (62.4 g-AI.L^{-1})	3200	100
585 solvent oil	3600	-

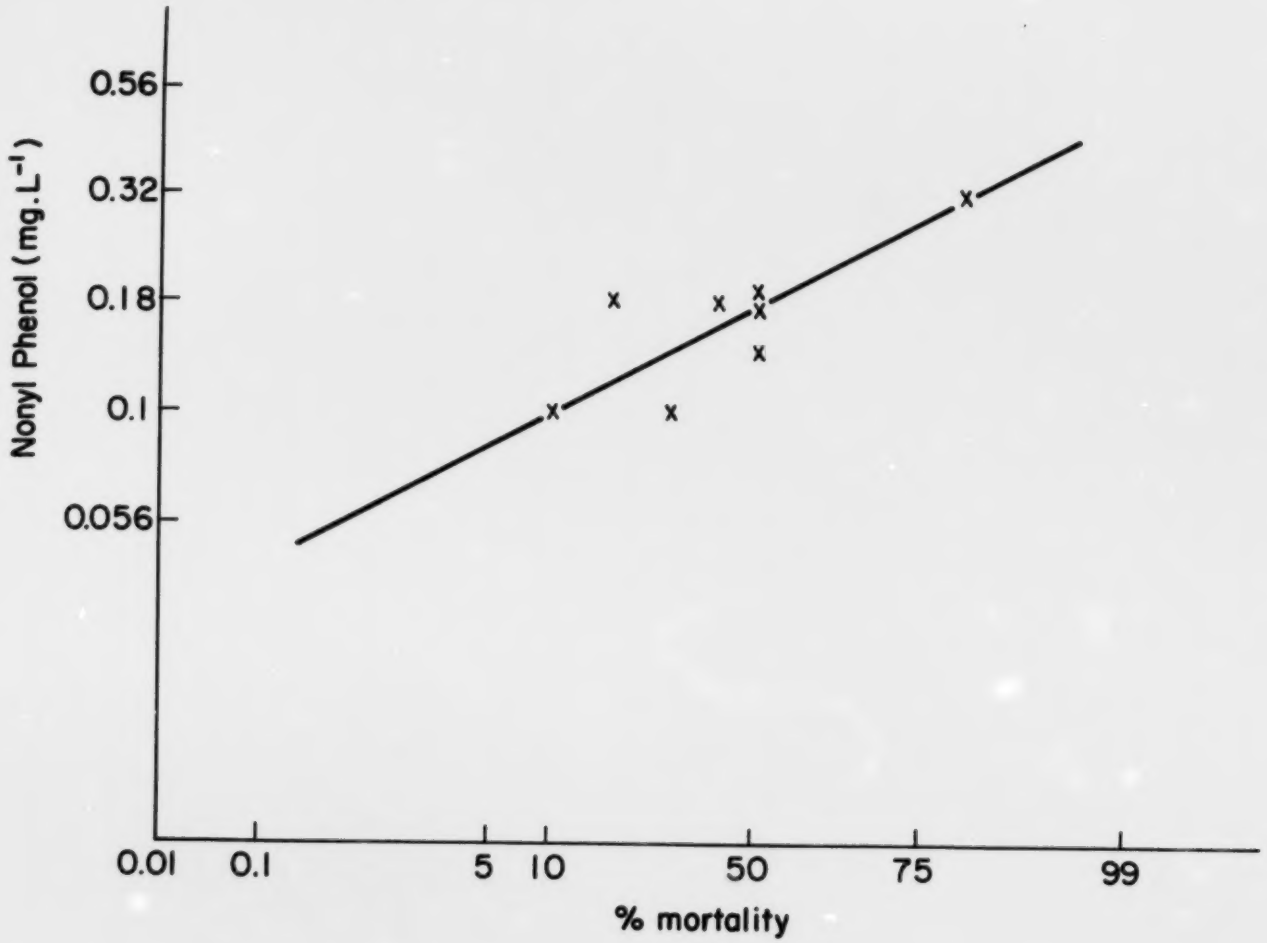

Figure 4-3. Toxicity of nonyl phenol to Daphnia pulex after 1 d exposure and subsequent transfer to clean water in static tests (Environmental Protection Service 1981).

McLeese et al. (1980b) determined the 96-h LC_{50} of the 1.8D formulation to the marine shrimp Crangon septemspinosa as 0.55 $mg.L^{-1}$. For the components of the formulation they determined 96-h LC_{50}'s for aminocarb to be 0.2 $mg.L^{-1}$, for nonyl phenol, 0.4 $mg.L^{-1}$, and for 585 solvent oil, 5.0 $mg.L^{-1}$. For another shrimp, Pandalus montagui, they tested only 585 solvent oil, and found a 96-h LC_{50} of 0.2 $mg.L^{-1}$. McLeese et al. (1981) determined the 96-h LC_{50} of nonylphenol to Crangon septemspinosa to be 0.3 $mg.L^{-1}$ (lethal threshold 0.15-0.32 $mg.L^{-1}$). Lowe (1962), using Bayer 44646, determined the LC_{50} for brown shrimp Penaeus aztecus to be 0.32 $mg.L^{-1}$ after both 24 and 48 h.

Guilbault et al. (1972) studied in vitro inhibition by aminocarb (probably technical) of cholinesterase of a fiddler crab and of a crayfish. They did not state the species of either animal. The I_{50} concentration for crab cholinesterase was 1.1×10^{-2} M (~ 2300 $\mu g.L^{-1}$) and for 10% inhibition the concentration was 4.5×10^{-5} M (~ 3 $\mu g.L^{-1}$). The crayfish cholinesterase I_{50} concentration was 1.0×10^{-2} M (2100 $\mu g.L^{-1}$) and for 10% inhibition the concentration was 1.6×10^{-5} M (3 $\mu g.L^{-1}$). Sundaram and Szeto (1979) determined a 96-h LC_{50} for the crayfish Orconectes limosus of 32.7 $mg.L^{-1}$ (95% CI[α] of 23.5 and 40.1 $mg.L^{-1}$). They used aminocarb in ethanol, which they added to the same river water from which they collected their test animals. They contrasted this LC_{50} with residues of 2.1 and 1.9 $\mu g.L^{-1}$ found by Sundaram et al. (1976) in stream water 0.6 d after aerial spraying at 70 $g.ha^{-1}$. Sundaram and Szeto (1979) checked their test animals for residues and metabolites and found that after exposure to 0.1 $mg.L^{-1}$ for 144 h the crayfish tissue contained 0.007 $mg.kg^{-1}$ of the parent compound and no detectable 4-methylamino or 4-amino analogues. The residues in the tissue were always proportional to but below the aminocarb residues in the water.

For the lobster, Homarus americanus, McLeese et al. (1980b) determined a 96-h LC_{50} of 0.2 mg nonyl phenol.L^{-1}. The other components of the aminocarb formulation were not tested.

All of these toxicities to Crustacea are low when related to the dosages of aminocarb and nonyl phenol expected in the field from spraying at 70 $g.ha^{-1}$. Although a few toxic concentrations of aminocarb approach concentrations found in the field, residues in the field are transitory. Among Crustacea, sensitivity seems to decrease in the order: scuds, water fleas, shrimp and crayfish.

4.4.2.8 Insecta

In static tests, Woodward and Mauck (1980) determined the 96-h LC_{50} for field-collected stonefly larvae, Pteronarcella badia, to be

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[α] CI - confidence interval.

28 (18-43, 95% CI) $\mu g.L^{-1}$ at pH 6.5 using technical aminocarb (98%). At pH 7.5 the LC_{50} was 19 (15-26, 95% CI) $\mu g.L^{-1}$ and at pH 8.5, 26 (20-33, 95% CI) $\mu g.L^{-1}$. They dissolved the aminocarb in acetone, diluted it with demineralized water, and adjusted the pH with reagent grade salts, mineral acids or bases.

Estenik and Collins (1979) reported a 24-h LC_{50} for Chironomus riparius of 376 (330-428, 95% CI) $\mu g.L^{-1}$. With piperonyl butoxide this rose to 1172 $\mu g.L^{-1}$ to give a synergistic ratio of 0.32. They were primarily concerned with the procedures and with the interaction of the oxidase and a number of insecticides.

Eidt (1979) conducted a simple laboratory test in stream water with an experimental aminocarb emulsifiable concentrate that did not contain an alkyl phenol. The formulation was highly toxic to Baetis spp. mayfly nymphs even at 1 μg aminocarb.L^{-1}; a blank, which lacked aminocarb, was toxic at an equivalent concentration of 10 μg aminocarb.L^{-1}.

4.4.2.9 Amphibia

The only major aquatic organisms, except fish, that have been checked for sensitivity to aminocarb or components of the field formulation are some frogs (discussed in Section 4.3.3) and tadpoles.

Lyons et al. (1976), in a carefully controlled laboratory experiment using 75% wettable powder, determined the 24-h LC_{50} for green frog tadpoles, Rana clamitans, as 247 (232-262, 95% CI) mg-AI.L^{-1} for small larvae and 234 (223-246, 95% CI) mg-AI.L^{-1} for large larvae. The 96-h LC_{50} was 118 (112-125, 95% CI) mg-AI.L^{-1} for small larvae. Lyons et al. (1976) were among the first to suspect that the formulation used in forest spraying might be more toxic than technical aminocarb. They speculated that the lower toxicity to tadpoles than that found for Atlantic salmon, Salmo salar, by Nigam (1975) may have been due to the formulation used.

4.4.3 FIELD MONITORING OF AQUATIC ORGANISMS OTHER THAN FISH

Prior to 1978, several formulations were used in field trials but operational sprays were usually solutions of aminocarb in nonyl phenol, further diluted with No. 2 or No. 4 fuel oil. In 1978 the diluent was changed to 585 oil. Field studies of the effects of various formulations on aquatic organisms other than fish are summarized in Table 4-11. With the circulation in 1979 of an unpublished report by Zitko (later incorporated in McLeese et al. 1980b) that the primary solvent, nonyl phenol, was more toxic to Atlantic salmon than aminocarb, concern developed about the biological activity of the so-called

Table 4-11. Field studies of effects of aminocarb on aquatic organisms other than fish.

Aminocarb Treatment	Rate g-AI.ha^{-1}	Medium	Peak residue (AI)[α]	Biological[β] compartment	Reference[γ]
Bayer 44646	1000	reservoir	-	chironomid emergence	Anderson et al. (1965)[δ]
aminocarb in Dowanol TPM	85	stream	-	benthos	Penny (1971a)
aminocarb in Panasol or as wettable powder in summer oil	103	stream	-	benthos	Penny (1971b)
formulation in fuel oil	2x52	stream, pond	-	benthos	Buckner et al. (1975), Buckner and Sarrazin (1975)
formulation in fuel oil	168	stream	-	benthos, drift	Rabeni and Gibbs (1976)
fenitrothion E.C. + formulation in fuel oil	210F+70+70	stream	-	benthos, drift	Gillis (1978); Montreal Engineering Co. Ltd. (1978)
formulation in fuel oil	70+70	stream	-	benthos, drift	Buckner et al. (1976)
formulation in fuel oil	70	stream pond	2.1 µg.ha^{-1} 1.9 µg.ha^{-1}		Sundaram et al. (1976)
formulation in fuel oil	70+70	3 streams	0	benthos, drift	Gillis (1978); Montreal Engineering Co. Ltd. (1978)
fenitrothion E.C. + formulation [in fuel oil?]	280F+280F+ 70	lake stream	0.9 µg.L^{-1} >1 µg.L^{-1}	benthos, plankton benthos, drift	Kingsbury (1978), Kingsbury and McLeod (1979), Mathieu and Provencher (1978), Sarrazin (1977), Lemieux (1977)
formulation in fuel oil + fenitrothion E.C.	90+210F+ 210F	stream	19-24 µg.L^{-1}	benthos, drift	Coady (1978)
formulation in fuel oil	70+70	beaver ponds	trace to 8 µg.L^{-1}	nekton	Whitman (1978)
formulation in S85	53 and 70	streams lake	3.34 µg.L^{-1} 5.709 µg.L^{-1}	benthos, drift, fish stomach contents	Sarrazin (1978), Holmes (1979)
formulation in S85	70	stream	-	drift	Osborne (1981)
formulation in S85	170 x 10^{-3}	stream	-	benthos, drift	Brown (1978), Brown (undated)

Table 4-11. (Cont'd).

Aminocarb Treatment	Rate g-AI.ha^{-1}	Medium	Peak residue (AI)[α]	Biological[β] compartment	Reference[γ]
formulation in fuel oil	4.7 µg-AI.L^{-1}	stream	4.7 µg.L^{-1}[ε] (2 h, 40 min)	drift, caged Leuctra	Eidt (1979)
formulation in 585	33.7 µg-AI.L^{-1}	stream		drift	Eidt (1979)
emulsifiable concentrate	8 µg-AI.L^{-1}	stream	8 µg.L^{-1}[ε] (2 h, 10 min)	drift	"
formulation in 585	63	stream lake	-	benthos, drift benthos	MacCallum (1980)
	63 lakes and bogs		3 µg(0-25).L^{-1}		Gaboury (1980)
formulation in 585	700 280 140	ponds	up to 53 µg.ha^{-1}	microflora	Elner and Wildish (1981), Wildish (1980)
formulation in 585	70	lakes	4.5 µg.L^{-1} (surface), 12 µg nonyl phenol.L^{-1}		Ernst et al. (1981)
nonyl phenol in 585	467 mL-AI.ha^{-1}	stream	9.1 µg nonyl phenol.L^{-1}	benthos, drift	Holmes and Kingsbury (1980)
formulation in 585	175	stream		benthos, drift	"
formulation in 585		stream	30 µg.L^{-1} threshold	drift	Ahern (1980)[δ], Ahern and Leclerc (1981)

[α] Peak residue measured, except where noted otherwise.

[β] Benthos means standing crop and and sometimes also species composition. Drift is drift of benthos.

[γ] More than one entry indicates more than one study in the same area, or more than one report on the same work.

[δ] Contrary to the narrative conclusions of some authors there is no evidence of a biological effect in any of these studies, except that Anderson et al. (1965) got "practically no control" of nuisance chironomids, and Ahern (1980) and Ahern and Leclerc (1981) demonstrated increases in benthos drift at 30 µg.L^{-1} or higher.

[ε] Mean value.

"inactive ingredients". Only recently have reports been careful to specify the formulation in unambiguous terms and have toxicity studies included the additives.

The earliest reference to the use of aminocarb in water was by Anderson et al. (1965), who were seeking an effective agent with which to control nuisance midges. They applied Bayer 44646, of unspecified formulation, to a reservoir of unspecified depth at over 1000 g-AI.ha^{-1} and got "practically no control" of chironomid midges. The low toxicity to a midge found by Estenik and Collins (1979) may explain this result.

During the first field trials of aminocarb as an aerial forest spray in 1970 and 1971 in New Brunswick, effects on aquatic invertebrates were monitored because of previous severe side effects with DDT. In one study (Penny 1971a), about 6 km of a stream was monitored as it passed through a 1000 ha block sprayed twice with aminocarb (dissolved in Dowanol TPM (Kettela 1981)) at 85 g-AI.ha^{-1}. Using five 929-cm^2 Surber samples at least once a week from late May to mid-August, Penny was unable to detect any differences from a control stream, in numbers at the taxonomic order level or in total biomass, that were attributable to the insecticide.

The next year Penny again monitored streams in 5000 ha experimental plots (Penny 1971b). They were sprayed with aminocarb at 103 g-AI.ha^{-1} dissolved in Panasol, or as wettable powder suspended in summer oil (Kettela 1981). Five Surber samples were used on each sampling date and the insects identified to order. It was concluded that there were reductions in numbers of some taxonomic orders in both streams and of biomass in one, and Penny attributed this to the insecticide. He did not use spatial controls and the data, which are plotted on graphs as means of five samples without variances, are not statistically significant as presented. Claimed reductions in Plecoptera larvae coincide with a period of heavy emergence of many species.

Buckner et al. (1975) monitored aquatic invertebrates in a stream in Quebec that was operationally sprayed twice with aminocarb at 52 g-AI.ha^{-1}. The formulation used was not stated but, in 1974, the field formulation usually contained nonyl phenol and fuel oil. They concluded, with some uncertainty, that numbers of stonefly nymphs were reduced by the treatment. However, their data were expressed as mean numbers of organisms per 929-cm^2 Surber sample with standard deviations that exceeded the means. They did not sample before the first treatment, but their control stream yielded equally variable low numbers of insects and they saw no distressed insects. The same data and conclusions are given by Buckner and Sarrazin (1975). Buckner et al. (1975) found no effect on bottom fauna in a shallow pond in Ontario, from aminocarb aerially applied at 70 g-AI.ha^{-1}. However, the variances of the mean numbers of invertebrates in their samples were very high and they do not state how the pond was sampled.

In 1975, an intensively monitored field trial was conducted in Maine on three 388-ha blocks using aminocarb at 168 g-AI.ha^{-1} (Krucera et al. 1976). The formulation is likely to have contained nonyl phenol as the primary solvent and No. 2 and or No. 4 fuel oil as the diluent. If so, this is the highest rate of formulation containing nonyl phenol that has been used along with intensive environmental monitoring. From streams in these blocks Rabeni and Gibbs (1976) took nine 929-cm^2 Surber samples from each of three riffles, and set a drift net for 24 h on each sample date (day 1 or 2 before spray, and day 1 or day 2, day 30, and day 60 after spray). They separated living and dead drift organisms. There were no clear effects on benthos diversity. No measure of variance was used, but differences as great as 50% were found 3 d apart. One stream had an apparent increase in Plecoptera, but it was well within the range of variation shown for their controls. Rabeni and Gibbs (1976) attributed the differences among samples to Surber sampling error, but had no better means of estimating standing crop because their artificial substrate benthos samplers were vandalised. Differences between immediate prespray and immediate postspray samples of Paraleptophlebia mayflies, Leuctra stoneflies, Chironomidae (midges), and Simuliidae (black flies) indicated no trends. Drift of benthos varied as much after treatment as before. Insecticide concentrations in the water were not measured, but small residues found in fish tissue were thought to have been ingested with invertebrate food organisms (Marancik 1976).

Montreal Engineering Co. Ltd. (1976) monitored the benthos drift in a stream wholly within a New Brunswick operational spray area. The spray regime was 210 g fenitrothion.ha^{-1} followed by two applications of aminocarb at 70 g-AI.ha^{-1}. The fenitrothion was applied in aqueous emulsion and the aminocarb was formulated with No. 2 fuel oil. Aminocarb was reported to have no significant effect on drift, using both temporal and spatial controls, whereas fenitrothion was reported to induce statistically significant increases in both dead and live drift. Benthos sampling was unsuccessful and insecticide residues in the stream water were not determined. Buckner et al. (1976) also sampled stream benthos in New Brunswick in an area sprayed twice, two days apart, at 70 g-AI.ha^{-1} with aminocarb formulated with No.2 fuel oil. They reported no effect on drift or standing crop. However, they pooled three Surber samples which made the data statistically useless for comparing prespray and postspray samples.

Gillis (1978) and Montreal Engineering Co. Ltd. (1978) monitored stream invertebrates in an area sprayed operationally twice at 70 g-AI.ha^{-1} in 1977. Water from three streams studied contained no aminocarb using analysis sensitive to 10 µg.L^{-1} and capable of detection to 1 µg.L^{-1}. Benthos was sampled using pot samplers recessed into the stream bed because of the unreliability of the Surber (1936) method.

He found no statistical differences in standing crop or drift between the treatments and controls.

In Quebec in 1977, a large area was sprayed with aminocarb formulation at 70 g-AI.ha^{-1} following two sprays with fenitrothion at 280 g-AI.ha^{-1}. Aquatic systems, including a lake and several streams, were monitored. Kingsbury (1978) reported no population or species changes in lake zooplankton as compared with the observations of Laperle (1964) in a year without spraying. On the lake surface, Mathieu and Provencher (1978) found residues on 14 aluminum interception samplers of 2 to 4 mg.m^{-2}. They found residues in the water of up to 0.9 µg.L^{-1} within the first hour after spray, and indicated a diminution of concentration from 0.4 to 0.6 µg.L^{-1} at the surface to 0 at the bottom (below 8 m). They hesitated to put any interpretation on their observations of vertical distribution of the extremely low residues. They found higher concentrations of aminocarb in water in relation to the surface deposits than of fenitrothion. This was attributed to the greater water-solubility of aminocarb and its solvent nonyl phenol over that of fenitrothion and of its solvent Aerotex, pointing out that aminocarb is less volatile than fenitrothion. Mathieu and Provencher (1978) described a brief rise in aminocarb in a stream to >1 µg.L^{-1}. Kingsbury (1978) reported small increases in drift of invertebrates in the same stream after the aminocarb spray, but he made no comparisons with controls. The variations were within the normal range reported elsewhere by Kingsbury and others. Kingsbury pointed out that he could not identify differences in bottom fauna that might be associated with the aminocarb spray or the two fenitrothion sprays that preceded it. In the lake, using Ekman grab samples, no changes in benthos were observed that could be attributed to the sprays (Kingsbury 1978); Sarrazin (1977) gave a brief report on the same work and attributed the lack of sensitivity of the monitoring to the earliness of the season, water quality, and flooding. These reports suggest that a decline in baetid mayfly nymphs in the lake may have been due in part to the aminocarb spray. Unfortunately, the sampling data are sparse, have no measure of variance, and are without spatial control for comparison. Lemieux (1977) studied the effects on stream invertebrates in the same area, but would attribute no changes to the treatments because of the confounding influences of fluctuating temperatures and flood conditions. Mathieu and Provencher (1978) found it impossible to separate any effects of the aminocarb formulation from those of fenitrothion.

In Newfoundland in 1977, streams were monitored for immediate chemical influences of operational aminocarb (formulated with nonyl phenol and fuel oil) sprays (Coady 1978). A summary report was given by the Environmental Monitoring Committee (1979a). In areas where one application at 90 g-AI.ha^{-1} followed two of fenitrothion at 210 g-AI.ha^{-1}, it was not possible to distinguish any effect of aminocarb on aquatic invertebrates from that of fenitrothion. In areas where there were two applications of aminocarb at 90 g-AI.ha^{-1}, no effects on

aquatic invertebrates were seen using drift nets and Surber samplers. Drift sampling was intensive and thorough; nets were set for 20 min every 3 h during spray day and the days before and after. The number of Surber samples was not specified. Maximum aminocarb residues recorded in stream surface water were 19 and 24 $\mu g.L^{-1}$ within 3 to 4 h of spray application and residues diminished to undetectable levels in 15 to 20 h (Osborne 1981). Coady (1978) provided the most detailed account of the 1977 Newfoundland monitoring but apparently did not recognize the unsubstantiated nature of the conclusions (Penny 1971b; Buckner et al. 1975; Buckner and Sarrazin 1975) that significant reductions of aquatic invertebrates, particularly stoneflies, occurred after operational aminocarb sprays.

Concern has developed that forest spraying might have an indirect effect on black duck populations by killing aquatic insects in ponds (e.g. Whitman 1978). Ducklings depend heavily on aquatic insects during the first weeks of their life and food availability could be critical. Whitman (1978) sampled ponds in an area sprayed twice at 70 $g\text{-AI.ha}^{-1}$. He found residues in the pond water from trace to 8 $\mu g.L^{-1}$, but no major reduction of insects. Hall and Kolbe (1980) suggested that, since frogs are relatively resistant to cholinesterase inhibitors tadpoles might accumulate such pesticides to levels that would be lethal when they were consumed by ducks or carnivorous species. Hall and Kolbe (1980) report that tadpoles concentrate organophosphorus pesticides up to 60 times the levels in water. Rick and Price (1974) observed heavy mortality in trays of tadpoles of the wood frogs Rana sylvatica and Rana clamitans sprayed at 104 $g\text{-AI.ha}^{-1}$ in a forested area. However they did not use controls or residue analysis.

During operational spraying in Quebec in 1978, stream invertebrates were monitored by Sarrazin (1978) and by Holmes (1979). Sarrazin (1978) claimed a brief increase in drift of aquatic insect larvae such as mayflies, stoneflies, caddisflies, and true flies after aminocarb sprays at 53 $g\text{-AI.ha}^{-1}$ and 70 $g\text{-AI.ha}^{-1}$. He stated that Amphinemura stoneflies, Simulium black flies, and heptageniid mayflies are the most sensitive to aminocarb but he presented no data. Sarrazin sampled benthos with Surber samplers but he found no changes. He also reported increases in black fly larvae in trout stomach contents and increases in larvae of burrowing mayflies, crane flies, black flies, and chironomid midges in sculpin stomachs, but he inferred no cause and effect relationship with aminocarb. Holmes (1979) studied aquatic invertebrates in three blocks sprayed with three insecticide treatments, aminocarb formulated in nonyl phenol and 585 oil once at 53 $g\text{-AI.ha}^{-1}$, aminocarb twice at 53 $g\text{-AI.ha}^{-1}$ and fenitrothion (210 $g\text{-AI.ha}^{-1}$) followed by aminocarb (53 $g\text{-AI.ha}^{-1}$). In drift of invertebrates in streams he indicated a small increase in black fly larvae at one of two stations after one aminocarb spray. Insecticide residues at the time (3.34 $\mu g.L^{-1}$) were the highest recorded in any of the streams (Section 2.7.1). Nonetheless such a small increase in drift could have been due to any number of factors including disturbance by people wading upstream, where

fish, benthos and water sampling stations were located. For benthos, only four Surber samples were used and none of the changes in samples were significant. For example, a reduction in numbers of baetid mayfly nymphs in samples from the area sprayed twice with aminocarb after an earlier spray with fenitrothion, was not significant even at the 60% confidence level. This means that changes in the stomach contents of slimy sculpins collected during the spray period cannot be shown to be related to the aminocarb spray. Holmes (1979) concluded that the three insecticide treatments detailed above had little or no adverse effects on aquatic invertebrates. This thoroughly conducted and reported study unfortunately did not provide enough evidence either to suggest an effect of aminocarb on aquatic invertebrates, or to say that there was none.

Osborne (1979) monitored streams in Newfoundland in an area sprayed twice with aminocarb (70 g-AI.ha^{-1}) formulated with nonyl phenol and 585 oil, in 1978. He claimed an immediate increase in numbers of aquatic insects in drift after spraying, and a return to normal drift patterns in 24 h, a result also reported by the Environmental Monitoring Committee (1979b). However, the data on which these conclusions were based (Osborne 1981) do not support the claims made. For example, in one case the drift two days after spray was double that on the day after spray; such differences are well within background variation. Changes in diversity of drift after spray were mentioned (Osborne 1979) but species composition data were not provided and it was speculated that factors other than spray could have affected drift diversity. Osborne gave no data on stream discharge, temperature, or weather, either in the 1979 report or among the unpublished data on which the report was based.

In 1978, Brown (undated) monitored stream insects in a 1200 ha block in Maine, sprayed with aminocarb in 1978 at 170 g-AI.ha^{-1} (more than twice the usual operational rate). The formulation used was not specified but probably contained diluent 585 and nonyl phenol. They described a number of apparent changes in numbers (both increases and decreases) of genera and families of Trichoptera and of Chironomidae, but no change in Plecoptera and Ephemeroptera. They saw mostly seasonal changes that varied greatly from brook to brook; some of the brooks were dry by the second month after spray. There was no increase in drift of either aquatic or terrestrial arthropods at the time of spray. None of the differences in samples of benthos standing crop was outside the normal variations for samples of this kind. There was no water analysis for aminocarb and posttreatment samples were compared with pretreatment samples but not with controls.

In 1977, Eidt (1978, 1979, 1980a) injected a stream with aminocarb (formulated with nonyl phenol and No.2 fuel oil) at 4.7 µg-AI.L^{-1} for 1.5 h, followed, after 1.5 h, by 13.7 µg-AI.L^{-1} for 1 h. There was no effect on drift of aquatic invertebrates or on caged Leuctra spp. stonefly larvae. In 1978 the experiment was repeated at a

calculated rate of 33.7 µg-AI.L^{-1} (formulated with diluent 585 and nonyl phenol) again with no effect. Because of difficulties in mixing the oil-based formulation, the experiment was repeated using an emulsifiable concentrate supplied by Mobay Chemical Corporation. The actual amounts in the water were estimated to be 1 µg-AI.L^{-1} for 2 h 30 min, none for the next 1 h, followed by 8 µg-AI.L^{-1} or more for 2 h 10 min. There was no effect of the emulsifiable concentrate on the drift of aquatic insects although a laboratory test had shown it to be highly toxic at dosages as low as 1 µg.L^{-1} for 3 h.

Two streams were monitored in Ontario (MacCallum 1980) in areas sprayed with aminocarb (probably formulated with nonyl phenol and diluent 585) at 63 g-AI.ha^{-1}. Drift nets were used morning and evening, although the times were not given, and benthos was sampled using four Surber and four 15-cm stone samples at each sampling time. Two control streams were also sampled. MacCallum noted modest increases in drift after the treatment and attributed them to "the dominant" caddisfly larvae. The two drift peaks were within the range of variation among samples reported taken at other times before and after the treatment and in the controls. Without a measure of variance, the drift data are not adequate to say whether an effect occurred or not. MacCallum (1980) did not suggest that changes in benthos standing crop occurred in the streams, nor in a lake that was sampled with an Ekman grab (eight 225 cm^2 grabs per sampling time).

In Quebec, Gaboury (1980) surveyed water bodies for aminocarb residues within operational spray blocks. Benthos was not monitored and instead effort was concentrated on methodology for the surveillance of aquatic organisms (Ahern 1980). All the concentrations reported by Gaboury (1980) (Section 2.7.1) were far below those regarded as toxic by Ahern (1980).

Elner and Wildish (1981), Wildish and Elner (1981) and Wildish (1980) sprayed three small ponds at 140, 280 and 700 g-AI.ha^{-1} (formulation contained 19.3% aminocarb, 50.1% nonyl phenol and 30.6% 585 solvent oil). They used a portable mist blower from the perimeter of the ponds, a method that would deliver a greater amount to the pond surfaces than would most sprays from fixed-wing aircraft. A fourth pond served as a control; microorganisms in these ponds had been monitored for a year before treatment, and metabolite aminocarb residues measured in the ponds as discussed in Section 2.7.1. In all treatments aminocarb "had little effect on the microbial communities" and "no indications of Matacil caused effects on pond microbiology were found during long-term observations which continued for 1 y following spraying". All ponds had normal spring blooms and comparable peaks in algal numbers shortly after treatment. Benthic invertebrates were too sparse in core samples to draw any conclusions about effects on their numbers.

With the revelation that nonyl phenol was more toxic to Atlantic salmon than aminocarb (McLeese et al. 1980b), a great deal of interest developed in the solvents and diluents of the aminocarb

formulation. In addition to the laboratory studies of McLeese et al. (1980a,b) which had been reported earlier in summary form by Zitko et al. (1980), Wells et al. (1979) discovered that test solutions of the aminocarb formulation, aged for 10 d out-of-doors, became nonlethal to rainbow trout, even though there was no decrease in aminocarb content. They advised that the toxicity of the aminocarb formulation needed to be studied separately and in combination, in the laboratory and in the field, before the fate of the formulation in aquatic systems could be adequately assessed and understood.

Holmes and Kingsbury (1980) described in detail the impact on aquatic organisms of a field experiment designed to determine the environmental hazards of a maximum allowable spray of nonyl phenol (467 $mL.ha^{-1}$). This was the same experiment described in much less detail in the preliminary report of Armstrong and Kingsbury (1979). In a comparable block sprayed with aminocarb field formulation in 585 diluent oil at 175 $g\text{-}AI.ha^{-1}$, residues were not persistent in any compartment but some high local concentrations were measured (see Section 2.7.1). In the nonyl phenol-treated stream, they noted an increase in the number of black fly larvae caught in a 2 h drift net set one day after treatment, but no increase in a 20 min set begun at the same time. Their tabulated data indicate a catch about 20 times greater than usual. There were no other indications of a possible effect and the authors suggest that because drift numbers fluctuated considerably in the control stream, environmental factors, not nonyl phenol, might have been responsible. This one large sample could have resulted from something as simple as a person upstream wading. Sampling benthos, using four Surber samples or four 20-cm diameter stones, indicated no effect.

In the stream treated with the aminocarb formulation, Holmes and Kingsbury (1980) noted modest increases in drift of baetid mayfly nymphs, black fly larvae, chironomid larvae and pupae, stonefly nymphs, caddisfly larvae, riffle beetles and their larvae. Their appended data, however, are higher only in the 1.5-h postspray sample by only 3 to 10 times for total drift, riffle beetles, caddisfly larvae and baetid mayfly nymphs, and there was no measure of variance with which to test their differences statistically. The drift data were based on small numbers of organisms and it is highly unlikely the sample differences were due to poisoning of benthos by the treatment, because much larger doses (Eidt 1979; Rabeni and Gibbs 1976) had no effect. Apparent slight reductions in the mean numbers of some organisms in the first postspray benthos sample are of no significance because nearly all the standard deviations given are as large or larger than the means.

Much of the difficulty in assessing the possible impact of aminocarb on aquatic organisms in natural systems arises because of the limitations of the methods used. Slight changes in drift catches, particularly of organisms most prone to drift, can result from changes in streamflow and in light intensity, from diurnal rhythms and from stream bottom disturbances by people working in the stream. The natural

rhythms and disturbances are usually noticed, but the activities of inexperienced seasonal workers would be enough to cause small inexplicable drift surges. Such surges might be expected to occur more frequently following the time of spray because sampling activity is always greatest at that time.

Ahern (1980) was primarily concerned with developing techniques for injecting streams with predictable quantities of insecticide, with determining if respiration of microorganisms or organic detritus is affected by aminocarb, and with finding an order of sensitivity of aquatic invertebrates to aminocarb. He injected the aminocarb field formulation (containing 167 g-AI.L^{-1} in diluent 585 and nonyl phenol); he did not analyze water samples, but based his concentrations on the amounts injected. Unexplained was how the oil-based solution mixed with the stream water. He incubated forest leaf litter in the streams for various times, then placed it in a flask in stream water with a film of oil on the surface to isolate the system from the atmosphere. He determined respiration rates as the O_2 change in the stream water. He found that below 20 µg-AI.L^{-1} injected for 24 h there was no effect on respiration of the microorganisms on the litter. Only after injecting 100 µg-AI.L^{-1} for 24 h was O_2 consumption changed (Table 4-7). It increased significantly above background, perhaps due to nitrogen fertilization from aminocarb decomposition.

Effects on benthos were determined by Ahern (1980). He used only drift samples, but the sensitivity of the method was increased by separating living and dead drift. He interpreted a threshold of 30 µg-AI.L^{-1}, based on the injected amount, for increase in drift. The effect was to increase total and dead drift in proportion to the abundance of major taxa in normal drift. The increase occurred as soon as injection began, diminished in the interval between successive injections, reoccurred when injection began again, and rapidly returned to pretreatment levels when treatment ceased. The increase, in total, was almost entirely due to the dead drift; live drift changed little. Two indices of sensitivity used did not distinguish between increases in drift due to factors with other than aminocarb and the values given were not applicable to other toxicants. The next year Ahern and Leclerc (1981) confirmed the threshold of 30 µg-AI.L^{-1} for increase in drift, and further noted that the amount of drift increased up to concentrations of 120 µg-AI.L^{-1}, after which there was no further increase.

Holmes (1981) applied three formulations, including two aminocarb 1.8F formulations, directly to a stream. The preliminary data suggest that 1.8F formulations have no greater effect on drift than does the 1.8D formulation.

4.4.4 SUMMARY OF AQUATIC IMPACT

The relative toxicity of aminocarb to a wide range of aquatic organisms has been established in laboratory tests. The crustaceans

tested were the most sensitive, followed by stonefly larvae. Plants, fungi and bacteria were the least sensitive. It appears likely that phytotoxic concentration of nonyl phenol might be expected in shallow, stagnant water following spraying at 70-g.AI.ha^{-1}. Most studies have been in streams where mixing and flushing may be rapid, but both lakes and ponds in operational spray areas have been monitored. Where fenitrothion and aminocarb have been used in successive sprays in the same area, toxic effects of fenitrothion, but not of aminocarb, on benthos, plankton and nekton have been noted.

Attempts to detect changes in benthos standing crop generally used too few samples and the Surber (1936) method, which has been shown to be inadequate to detect any but gross changes in standing crop (Needham and Usinger 1956; Chutter and Noble 1966; Chutter 1972). In many reports, mean benthos densities are given with larger standard deviations, which reduces the chances to less than 60% that differences among means are real. Aquatic habitats are extremely variable and stream bed habitats in particular change drastically over short distances. Nonetheless, samples of drifting benthos, which are sensitive to changes resulting from perturbations, have not demonstrated a toxic effect of operational sprays.

The only field studies in which a toxic effect of the aminocarb formulation on aquatic organisms has been demonstrated are those of Ahern (1980) and Ahern and Leclerc (1981) which suggest a threshold of 30-µg AI.L^{-1} for drift of benthos and a threshold of about 100 µg-AI.L^{-1} for 24 h for effects on O_2 consumption by microorganisms on litter.

Wells et al. (1979) suggested that the formulation is more toxic than aminocarb and McLeese et al. (1980a,b) clearly demonstrated this in laboratory tests. Nonyl phenol, which has constituted over 50% by weight of the undiluted aminocarb formulation, compared with about 19.5% for aminocarb, was shown to be nearly as toxic as aminocarb. Holmes and Kingsbury (1980) conducted a field experiment in which nonyl phenol was sprayed at the maximum allowable rate. Careful monitoring showed some high residues, but no toxic effects on benthos in drift or in situ. On the basis of preliminary data, the "flowable" (1.8F) formulation appears to be less toxic to fish than formulations containing nonyl phenol (see Table 4-7). Most field studies on the effects of aminocarb on aquatic organisms have involved formulations containing nonyl phenol and 585 oil. Thus the lack of observed toxic effects on aquatic organisms occurred in spite of the use of nonyl phenol and oil.

Varty (1980) identified, as major impediments to risk assessment, the spatial variability of pesticide deposit and the complex relationship between residues in substrates and the response of fauna (and flora). Maguire (1980) warned of the hazard presented by concentration of pollutants in the surface microlayer; surface breathing insects and vertically migrating nekton may be at risk. Others have warned, although not in print, that laboratory-determined

toxicities, deemed low in terms of observed residues in water or sediments, may be cause for concern if a pesticide strongly partitions to the niches of the organisms concerned. The principal gap in our knowledge of the possible hazard to aquatic organisms is the partitioning and fate of aminocarb and its metabolites in the aquatic habitat. More knowledge of the distribution and fate of aminocarb and its metabolites is needed. Monitoring studies that could detect ecological impact, through action on the invertebrate community have been limited.

5.0 MAMMALIAN TOXICITY

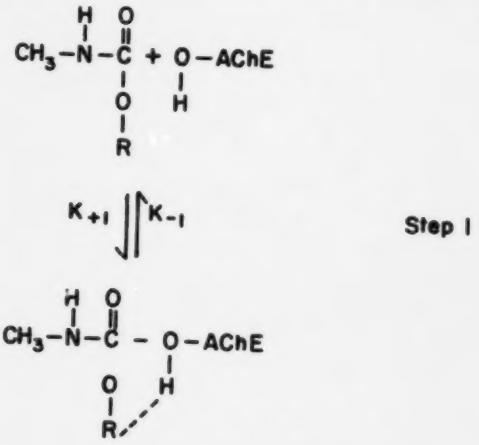
To characterize the toxicity of a pesticide, numerous studies must be conducted; they involve a variety of animal species exposed by several routes of administration for different periods of time. Carbamate insecticides, a class of which aminocarb is a member, are known to inhibit the enzyme cholinesterase. Clinical experience with carbamates demonstrates that their toxic effects can be ascribed to this inhibition.

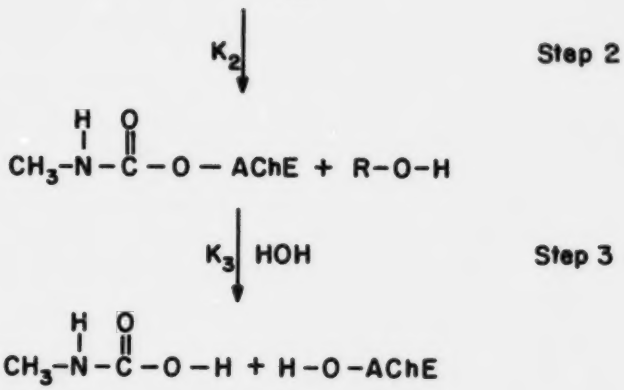
Cholinesterase is a critical enzyme because of its essential role in the process of transmission of the nerve impulse across many synaptic junctions. At these "cholinergic" junctions, acetylcholine is the chemical neurotransmitter; it is released by the prejunctional membrane, diffuses across the narrow junctional cleft and excites the postjunctional membrane. To allow the latter to recover so that it can respond to the next nerve impulse, acetylcholine in the junctional cleft must be rapidly destroyed. Acetylcholinesterase serves this function. If it is inhibited, free acetylcholine accumulates in all organs, tissues and body fluids. In the synaptic cleft of cholinergic junctions, this buildup prevents repolarization and recovery of postjunctional membranes. The result is excessive stimulation of cholinergic receptors on the postjunctional membrane, causing the postjunctional effector cells to respond in an abnormally intense way. This excessive stimulation eventually induces a response failure of some (but not all) effector cells. The resulting signs and symptoms are described in Section 5.2.

5.1 MECHANISM OF CHOLINESTERASE INHIBITION

In order to understand both the acute toxic effects of cholinesterase inhibition and resulting treatment and the long-term effects on the neuron, it is necessary to know the differences in the mechanism of inhibition by carbamate and organophosphorus insecticides.

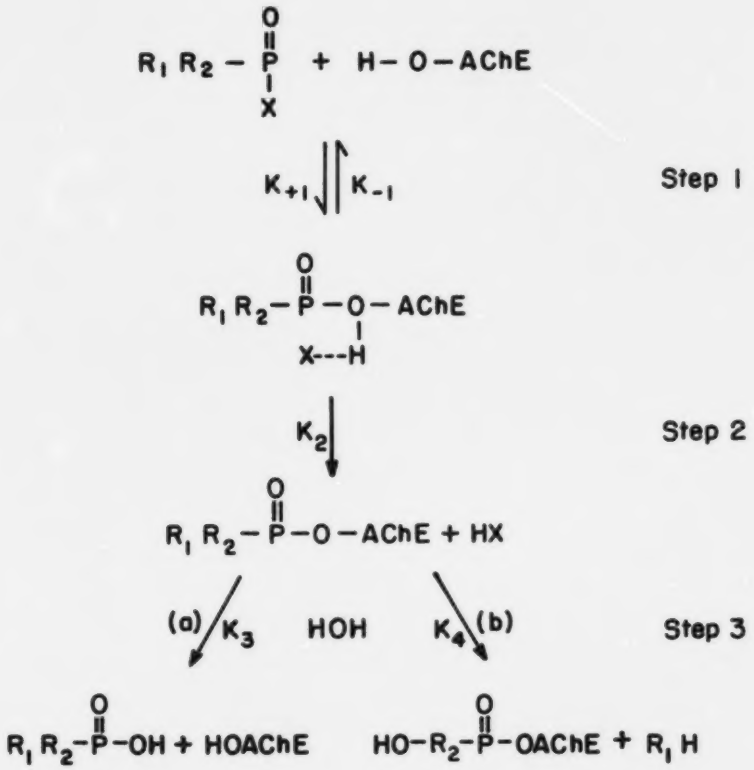
The way in which N-methyl- and dimethyl-carbamates inhibit acetylcholinesterase (AChE) is as follows (Kuhr and Dorough 1976):





Although carbamates have been referred to as reversible inhibitors of acetylcholinesterase, the term is incorrect since the carbamate is not regenerated intact but is, in fact, broken down to the corresponding carbamic acid (Steps 2 and 3). However, the rate of recovery of the enzyme is rapid.

The inhibition of acetylcholinesterase by organophosphorus compounds (OPs) is similar to the carbamate inhibition. However, there is one important additional step that may occur, that is called aging. The inhibition mechanism is as follows:



After formation of an enzyme substrate complex (Step 1), a second enzyme substrate complex is formed (Step 2) subsequent to which some dephosphorylation of the enzyme can occur as shown in Step 3a. A process known as aging may also take place in which a portion of the inhibited esterase undergoes cleavage, yielding an inactive enzyme with a very stable ionized phosphorus group (Casida and Baron 1976). Aldridge (1976) suggested two mechanisms for aging, one H^+-catalyzed through carbonium ion formation and the other through a part of the normal enzyme reaction hydrolyzing another ester bond. This aging reaction is not significant with carbamate inhibited esterases (Aldridge and Reiner 1972). Its importance will be discussed in more detail in Section 5.4 on delayed neurotoxicity.

The much slower regeneration of the organophosphorus inhibited acetylcholinesterase has led to the term irreversible inhibition. As with carbamate inhibition, the term is not altogether accurate. There are, however, marked differences in effects that are observed clinically following poisoning with carbamates and organophosphorus insecticides that are related to these rates and modes of regeneration of the enzyme.

It would be impossible to routinely monitor inhibition of acetylcholine in the neuron. However, acetylcholinesterase of the red blood cell (RBC) is similar to that of the nervous system, and changes in the activity of the RBC cholinesterase are thought to reflect changes similar to those in the nervous system. Carbamates and OPs also inhibit the plasma cholinesterase which is called pseudocholinesterase, the function of which is unknown. Severe depression of pseudocholinesterase appears to be without clinical significance.

5.2 CLINICAL MANIFESTATIONS OF CHOLINESTERASE INHIBITION

Whereas many reports fail to mention clinical signs of intoxication in acutely dosed laboratory animals, a few observations are available. Orally poisoned rats display typical symptoms of cholinesterase inhibition including tremors, muscle spasms, diarrhea, and so-called bloody tears (Mobay Chemical Corporation 1961). (The latter are almost certainly due not to red blood cells but to a heme pigment secreted by the rat's Harderian glands in response to many non-specific stresses.) These symptoms appear within a few minutes to a few hours after oral or intraperitoneal administration (DuBois and Raymund 1962a). Other signs reported in acutely poisoned rats include muscle fasciculations, lacrimation, diarrhea and rough coats (Nelson and Matzkanin 1977), the latter presumably due to piloerection. Convulsions have been mentioned (Nelson 1978d), but it seems likely that they were terminal and asphyxial in origin. The same cholinergic signs are encountered in rats and mice poisoned by the inhalation of aminocarb aerosols (Mobay Chemical Corporation 1961; Nelson 1978h). Similar signs and symptoms occur in poisoned rabbits (Crawford and Anderson 1972a) and chickens (Kruckenberg 1977).

Few, if any, pathologic lesions can be found in these acutely poisoned animals (Nelson 1978e). Congested lungs and liver are often described at necropsy (Nelson and Matzkanin 1977; Nelson 1978d, 1978f), but such changes are usually regarded as agonal and not indicative of any specific organ toxicity of the test substance. Extensive pulmonary pathology described in rats which survived an inhalation test (Nelson 1978e) probably represented preexisting disease.

No reports of aminocarb poisoning of human beings were found in the clinical literature. Occasionally workers in pesticide manufacturing plants are said (e.g. Everett 1965) to have experienced acute cholinergic symptoms, but the industrial experience has not been described. In plants manufacturing more than one carbamate pesticide, it is not always possible to identify which agent is responsible for sporadic instances of cholinesterase inhibition or cholinergic symptoms (Lamb 1981). The experience of pesticide applicators has also not been described. Hayes (1975) lists 10 cholinesterase-inhibiting carbamate pesticides that are reported to have caused illness in man; aminocarb is not among them.

While the issue of chronic poisoning is far from settled, the experimental studies in animals described above suggest that the major hazard of aminocarb to man is likely to be acute systemic poisoning, whatever the mode of exposure. No basis exists for postulating that the syndrome of acute intoxication induced in man by aminocarb is different from that induced by any other carbamate insecticide, except perhaps for small differences in the latency and duration of the illness. The clinical experience with carbaryl (summarized by Gosselin et al. 1976) and methomyl (Liddle et al. 1979) demonstrates that the toxic effects commonly produced by agents of this group can be ascribed to the consequences of in vivo cholinesterase inhibition.

Toxic signs and symptoms can be classified according to the tissue sites of cholinergic receptors. Acetylcholinesterase at these sites normally protects the receptors against excessively high concentrations of endogenous acetylcholine. This protection disappears when the esterases are inhibited. A "muscarinic" subset of cholinergic receptors controls the contraction of smooth muscles in most viscera and the secretion of many exocrine glands. Excessive stimulation of these smooth muscle receptors results in pupilloconstriction (miosis) with ocular pain and sometimes dimness of vision, bronchospasm with consequent dyspnea, and abnormal motility of the stomach and intestines with cramps, nausea and vomiting. Less commonly, piloerection and ciliary muscle spasm (ciliospasm) with blurred vision are encountered. Smooth muscle spasm is sometimes so intense that involuntary urination and defecation result. Hypersecretion is manifested as excessive salivation, sweating, tearing and the accumulation of both mucus and serous secretions in the respiratory and alimentary tracts. Pallor and either tachycardia or bradycardia may occur, as well as occasional arrhythmias and transient conduction defects within the heart.

Headache, weakness and giddiness may reflect hypotension and other circulatory derangements.

Cholinergic receptors of the "nicotinic" subset are found in autonomic ganglia and in the motor end plates of striated muscle. Initially these receptors are also activated by the normally high levels of endogenous acetylcholine that result from cholinesterase inhibition. Later, however, they become insensitive to acetylcholine and cease to function, particularly in severe poisonings when acetylcholine levels may become extremely high. Excitation of cholinergic receptors on striated muscle are responsible for the twitching and fasciculations sometimes observed. Receptor inactivation leads to generalized profound weakness and incoordination (e.g. slurred speech), with eventual paralysis even of the respiratory muscles.

Cholinergic receptors in the brain and spinal cord subserve many functions, and their excessive stimulation (in parathion poisoning for example) may be responsible for mental confusion, disorientation, drowsiness, convulsions, and coma, as well as vague neuropsychiatric disorders (e.g. nightmares) during the recovery period. Most carbamate insecticides, however, presumably including aminocarb (Section 5.8), do not appear to cross the mammalian blood-brain barrier fast enough to inhibit brain cholinesterase to a clinically significant extent.

Acute poisonings by carbamate pesticides, organophosphorus insecticides and nerve gases have many clinical features in common; the inhibition of cholinesterase is thought to be the common biochemical lesion responsible for all of the acute toxic effects. The principal distinction is the duration of the toxic state. Because carbamate-induced inhibition of cholinesterase recovers spontaneously at much faster rates than inhibition produced by organophosphorus agents (O'Brien 1960, 1968), the clinical illness subsides much more quickly. In carbaryl poisoning (Gosselin et al. 1976), symptoms may last only a few minutes and rarely, if ever, more than 8 h. Aminocarb may or may not be metabolized more slowly than carbaryl, but because the monomethylcarbamylated cholinesterases produced by the two agents are believed to be identical (O'Brien 1968), it is unlikely that a single exposure to aminocarb produces in man an illness of more than a few hours duration.

5.3 CLINICAL MANAGEMENT OF AMINOCARB POISONING

The principal aim of drug therapy in anticholinesterase poisoning is to protect cholinergic receptors against excessive stimulation by endogenous acetylcholine. Any of several reversible receptor blocking drugs might be adequate, but atropine is selected by almost every therapist. It acts on peripheral muscarinic receptors and on cholinergic receptors within the central nervous system but not on the nicotinic receptors of motor end plates. Thus, atropine serves to suppress the so-called "autonomic" manifestations of anticholinesterase

poisoning but not the muscle paralysis seen in severe poisonings. Nevertheless, atropine alone is often judged to be life-saving; in laboratory tests it has protected animals against many mean lethal doses of organophosphorus poisons (O'Brien 1960) and carbamate insecticides (Kuhr and Dorough 1976). For example, pretreatment of female rats with an intraperitoneal injection of atropine sulfate (100 $mg.kg^{-1}$) 10 min before intraperitoneal aminocarb, increased the LD_{50} of aminocarb from 13.4 to 55 $mg.kg^{-1}$ (DuBois and Raymund 1962b). Victims of anticholinesterase poison are tolerant of atropine and require large and repeated doses of it. With adult human patients, intramuscular or intravenous doses of 1 to 4 mg atropine sulfate are commonly recommended (e.g. Gosselin et al. 1976), repeated as necessary at intervals of a few minutes, until signs of excess cholinergic activity, such as intense salivation, are suppressed.

A secondary aim of drug therapy is to promote restoration of cholinesterase activity by accelerating, if possible, hydrolysis of the phosphoryl or carbamyl ester bond which blocks enzyme activity. Pralidoxime chloride (2-PAM) is marketed for this purpose but is not recommended for carbamate poisoning. Given alone, it failed to protect rats against aminocarb (DuBois and Raymund 1962b) or carbaryl (Carpenter et al. 1961) although it was mildly effective against some other carbamates (Natoff and Reiff 1973). Given with atropine, it appeared to enhance the toxicity of carbaryl, but was slightly antidotal against most other carbamates tested (Natoff and Reiff 1973). In organophosphorus poisoning, however, it has proven to be a distinctly useful adjuvant to atropine (Gosselin et al. 1976; Hayes 1975). Whether or not it is ever useful against insecticidal carbamates in patients adequately atropinized is a controversy. Its ability to speed the in vitro hydrolysis of the carbamyl ester bond of monomethylcarbamylated cholinesterase is not impressive. For example, after exposure to carbaryl or several other active monomethylcarbamates, the half-recovery time of bovine erythrocytic cholinesterase was 23 min at 38°C in the presence or absence of 10^{-4} M 2-PAM (O'Brien 1968). Fortunately, atropine alone is usually adequate to control signs and symptoms in poisonings due to carbamate pesticides (Gosselin et al. 1976). The transient nature of the usual intoxication provides little opportunity to test other ancillary antidotes.

Various nonspecific measures of supportive therapy are also important in managing victims of anticholinesterase poisoning. In the presence of central or peripheral respiratory paralysis, artificial respiration is necessary to sustain life. Similarly, suctioning may be required to clear respiratory tract mucus and to keep the airway open. The details of supportive therapy are discussed in various treatises of clinical toxicology (e.g. Gosselin et al. 1976).

5.4 DELAYED NEUROTOXICITY

The delayed neurotoxic effect which may occur following exposure to a few specific organophosphorus insecticides is in no way

related to the cholinergic effects which result from the inhibition of cholinesterase and the concomitant buildup of acetylcholine within the synapse (Cavanagh 1973). Although the mechanism of delayed neurotoxicity is not fully understood, it is currently believed that aging of the neurotoxic esterase enzyme plays a key role in the genesis of the pathologic lesion since only those pesticides which cause such aging have been shown to be capable of inducing lesions.

Early work by Johnson (1969a,b, 1970) identified an esterase which he called neurotoxic esterase (NTE) that was membrane bound in nervous tissue. It was initially thought that inhibition of NTE led to the observed neuropathy (Johnson 1969a). The fact that inhibition of NTE did not always result in neuropathy suggested that other factors were involved (Johnson 1970) and it has been proposed that a process of aging of NTE occurs after inhibition by neurotoxic agents (Johnson 1976). Although the actual mechanism for the axonal degeneration has not yet been fully elucidated, NTE activity has been shown to be an effective biological monitor (Lotti and Johnson 1978; Johnson 1980). In fact, these authors propose that measurement of the degree of inhibition of acetylcholinesterase and NTE enables a scale of biochemical response to be constructed. Compounds such as carbamates, phosphinates and sulphonates, which produce inhibited enzyme but which do not age, do not cause neuropathy (Johnson 1970) and actually protect *in vivo* against challenge doses of compounds which can produce neuropathy (Lotti and Johnson 1978).

All new pesticides causing acetylcholinesterase depression, or structurally related to compounds known to induce delayed neurotoxicity, must be tested for their potential to induce delayed neurotoxicity using the adult domestic hen. Examples of compounds that must be tested are organophosphorus pesticides and carbamates other than methyl- and dimethylcarbamates (Federal Register 1978). The hen was selected as the species of choice because of its sensitivity to neurotoxic chemicals and the striking similarities in the response seen in the hen and in humans following poisoning incidents (Smith *et al.* 1930a, 1930b; Albertini *et al.* 1968). The suggested protocol for an acute delayed neurotoxicity test is as follows. Adult domestic hens are dosed at the LD_{50} dose and protected with atropine and/or 2-PAM to carry them over the initial cholinergic phase of the exposure. After recovery the hens are then monitored daily for signs of ataxia, and if no signs appear by about day 21, they are then dosed again and monitored for a second 21 days. The positive control group is dosed with triorthocresyl phosphate (TOCP). Multiple longitudinal and cross sections of cervical, thoracic and lumbar regions of the spinal cord and sciatic nerve are examined. The lesions that may occur involve a focal distal, but not terminal, axonal degeneration (Bouldin and Cavanagh 1979). This information would suggest that the traditional hypothesis of retrograde degeneration is incorrect. The effects have been seen more consistently in the cholinergic fibres of the spinal cord (Abou-Donia and Graham 1978, 1979). In fact, Abou-Donia and Graham (1978) state that "the sum of our

experience to date in working with delayed neurotoxicity (organophosphorus compounds) is that one could achieve histological verification solely through study of the spinal cord stained with myelin, nuclear, and cytoplasmic stains such as hematoxylin-eosin and luxol-fast-blue." While peripheral nerve lesions are dramatic when present, they have been encountered "rarely". Recently, it has been suggested (OECD 1982) that the medulla oblongata and proximal sections of the fibril nerve would be useful and definitive sites to section and study.

Although N-methylcarbamate pesticides, such as aminocarb, are not required to be tested for delayed neurotoxicity (Federal Register 1978), a number of studies have been conducted on aminocarb. In one study (Kimmerle 1965), adult hens were given feed containing 0, 250, 500, 1000 and 2000 mg.kg-diet^{-1} of technical aminocarb for 30 d. They were then put on normal feed (no aminocarb) and observed for an additional 28 d for neurotoxic signs (weakness in legs, limping, inability to walk). Although dose-related effects were observed in body weight, mortality and cholinesterase activity, no delayed neurotoxic effect was reported. Test animals put on recovery reached the weight of the control animals and cholinesterase activity returned to normal. No histopathology was reported. Careful clinical evaluation of the hens for abnormalities in gait and balance should provide sensitive indicators of underlying neurological disturbances which appear along with histopathological changes.

Gaines (1969) reported that aminocarb tested in adult hens did not cause paralysis. In a more recent study (Kruckenberg 1978), twenty adult hens were orally dosed at the LD_{50} level (74 mg.kg-BW^{-1}) and protected by an intramusclar dosage of 50 mg.kg^{-1} atropine sulfate. The carrier control group of 5 hens was administered polyethylene glycol at 0.1% of their body weight, and the positive control group of 5 hens was orally dosed with 500 mg.kg-BW^{-1} TOCP. The hens were observed daily for signs of neurotoxicity and were dosed again on day 30 and observed for an additional 30 d. The sciatic nerves in their entirety, spinal cords and brains of the control birds and six randomly selected test birds were fixed and stained with luxol-fast-blue and hematoxylin-eosin. No clinical signs were observed in any carrier control or aminocarb treated hens. All positive control (TOCP) hens became paralyzed. There were no histopathological changes in the aminocarb-treated birds other than the occasional neuron showing evidence of Wallerian degeneration. These were similar to changes seen in carrier control birds. The TOCP-treated birds showed Wallerian degeneration most frequently in cross sections of the spinal cord. This study was conducted in an acceptable manner, and there was no evidence to suggest that aminocarb caused delayed neurotoxicity.

It has also been suggested that detailed studies of nerve conduction velocity (NCV) would be useful in diagnosing neurotoxic effects following exposure to cholinesterase inhibitors in the test

animals. This is questionable in cases of exposure to delayed neurotoxic compounds which cause primarily axonal degeneration with secondary demyelinating effects. The slight decreases in NCV observed in test animals may reflect the loss of the fastest conducting fibres only, and marked changes in velocity are not observed before drastic pathological changes have occurred (Fullerton and Barnes 1966), thereby minimizing the value of the test to detect early changes in function of the neuron.

The nonspecific changes (which are unlikely to be related to delayed neurotoxicity) reported by Jager (1976) appear to be useful in monitoring exposure to workers in an industrial setting. The underlying mechanisms which leads to the changes in NCV and amplitude are as yet unexplained.

5.5 ACUTE TOXICITY

5.5.1 ACUTE TOXICITY IN RATS

Many studies have served to define the acute single-dose toxicity of aminocarb in laboratory mammals. Mean lethal doses (LD_{50}) for the white rat are summarized in Table 5-1. Although various formulations were used in these tests, in all cases LD_{50} values are stated as mg-AI.kg-BW^{-1}. In most of these single-dose tests, survivors were observed for 14 d before mortality rates were computed. Most of the nonsurvivors, however, died on the first or second day and deaths were almost never encountered beyond the third day. Table 5-1 shows that the LD_{50} varied with the formulation, the vehicle or diluent, the route of administration and perhaps the sex. Except for the route of administration, these variables did not introduce large variations in the lethal dose. Inhalation data are summarized later (Table 5-3).

With respect to the oral route (gavage), the more recent and more precise tests (tests no. 12 - 21 in Table 5-1) yielded LD_{50}s between 20 and 30 mg.kg-BW^{-1}. In most of these trials various oil-soluble concentrates were tested, and they were usually dispersed in polyethylene glycol. When dissolved in peanut oil (tests no. 9 and 10), or administered as a 50% wettable powder in aqueous suspension (test no. 6), aminocarb appeared to be significantly less toxic (although the apparent peanut oil effect may mean only that Sherman strain rats are more tolerant to aminocarb than are Sprague-Dawley rats). In contrast, the addition of diesel oil enhanced the toxicity as represented by a reduction in the LD_{50} (cf. tests no. 11 and 12, also 13 and 14). Recrystallized (test no. 5) and analytical grade (test no. 18) aminocarb were not appreciably more or less toxic than the usual technical grade (e.g. test no. 17).

Aminocarb is distinctly more toxic via the intraperitoneal route than by mouth. As noted in Table 5-1, the LD_{50} values are essentially the same for all tested formulations.

Table 5-1. Acute toxicity of aminocarb in laboratory rats.

Test No.	No. Rats	Sex	LD_{50} mg-AI.kg-BW^{-1}	95% Confidence limits	Formulation (% AI)	Vehicle[n] (diluent)	Reference
					Oral (gavage)		
1	32[α]	M	50		99% technical (99%)	1	Mobay Chemical Corp. (1961)
2	35[β]	M	30		Bayer 44646 (presumably >95%)	2	DuBois and Raymund (1962b)
3	35[β]	F	30		Bayer 44646 (presumably >95%)	2	DuBois and Raymund (1962b)
4	25[β]	F	30		(1.5 lb/gal) spray concentrate (16.5%)	2	DuBois and Raymund (1962a)
5	22[β]	F	30		Recrystallized (presumably 100%)	2	DuBois and Raymund (1962a)
6	24[β]	F	35		50% wettable powder (50%)	3	DuBois and Raymund (1962a)
7	30[γ]	M	19.8	± 1.1	Liquid formula (34%)[ε]	2	DuBois (1968)
8	30[γ]	F	19.0	± 1.2	Liquid formula (34%)[ε]	2	DuBois (1968)
9	40[δ]	M	40	29-56	Technical (presumably >95%)	4	Gaines (1969)
10	70[δ]	F	38	33-44	Technical (presumably >95%)	4	Gaines (1969)
11	20[α]	M	45	29.7-68	1.4 oil-sol. concentrate (18%)	2	Crawford and Anderson (1972b)
12	20[α]	M	25.5	16.9-38.5	1.4 oil-sol. concentrate (18%)	5	Crawford and Anderson (1972b)
13	20[α]	F	26	18.4-37.6	1.4 oil-sol. concentrate (18%)	2	Crawford and Anderson (1972b)
14	20[α]	F	17.1	14.1-20.8	1.4 oil-sol. concentrate (18%)	5	Crawford and Anderson (1972b)
15	40[γ]	M	22.5[ζ]	19-26.8	1.4 oil-sol. concentrate (18%)	6	Nelson and Matzkanin (1977)
16	40[γ]	F	21[ζ]	17.8-25.4	1.4 oil-sol. concentrate (18%)	6	Nelson and Matzkanin (1977)
17	80[γ]	F	27	23-31	Technical (presumably >95%)	6	Nelson (1978d)
18	80[γ]	F	22	19-25	Analytical (presumably >99%)	6	Nelson (1978d)
19	80[γ]	M	33[ζ]	28.5-39	Matacil 1.8 - 585 (19.5%)	6	Nelson (1978e)
20	80[γ]	F	19.7[ζ]	16.2-24.8	Matacil 1.8 - 585 (19.5%)	6	Nelson (1978e)
21	40[γ]	F	26.9[ζ]	22.8-31.8	Matacil 1.8D Canada (19.5%)	6	Nelson (1978f)
					Intraperitoneal		
22	29[α]	M	21	± 3	99% technical (99%)	1	Mobay Chemical Corp. (1961)
23	34[β]	M	13		Bayer 44646 (presumably >95%)	2	DuBois and Raymund (1962b)

Table 5-1. (Cont'd).

Test No.	No. Rats	Sex	LD_{50} mg-AI·kg-BW^{-1}	95% Confidence Limits	Formulation (% AI)	Vehicle[n] (diluent)	Reference
					Intraperitoneal		
24	36[β]	F	13.5		Bayer 44646 (presumably >95%)	2	DuBois and Raymund (1962b)
25	25[β]	F	19		(1.5 lb/gal) spray concentrate (16.5%)	2	DuBois and Raymund (1962a)
26	25[β]	F	17		Recrystallized (presumably 100%)	2	DuBois and Raymund (1962a)
27	25[β]	F	17.5		50% wettable powder (50%)	3	DuBois and Raymund (1962a)
					Dermal		
28	20[β]	F	275		Bayer 44646 (presumably >95%)	7	DuBois and Raymund (1962b)
29	24[β]	F	148		(1.5 lb/gal) spray concentrate (16.5%)	2	DuBois and Raymund (1962a)
30	20[β]	F	300		Recrystallized (presumably 100%)	2	DuBois and Raymund (1962a)
31	5[β]	F	500		50% wettable powder (50%)	none	DuBois and Raymund (1962a)
32	30[γ]	F	501	±34.6	Liquid formula (34%)[ε]	*	DuBois (1968)
33	34[γ]	M	479	±30.8	Liquid formula (34%)[ε]	*	DuBois (1968)
34	40[δ]	M	280	257-305	Technical (presumably >95%)	8	Gaines (1969)
35	40[δ]	F	320	269-381	Technical (presumably >95%)	8	Gaines (1969)

[α] Unspecified strain.

[β] Sprague-Dawley.

[γ] Holtzman (Madison, Wisc.), Sprague-Dawley derived.

[δ] Sherman strain.

[ε] Although not specified in the original report, this formulation may contain 66% N-methyl-2-pyrrolidone.

[c] Derived from the original report, which specified mg. formulation only.

[n] Diluent:
1. Unspecified oil
2. 20% ethanol, 80% propylene glycol
3. Suspended in a 0.2% aqueous solution of carboxymethyl cellulose
4. Peanut oil
5. 1 vol. matacil: 2.5 vol. diesel oil, diluted with 20% ethanol, 80% propylene glycol
6. Polyethylene glycol (carbowax) (usually PEG-400)
7. Ethanol solution (100 mg.mL^{-1})
8. Xylene solution

Unlike most of the carbamate insecticides (Gaines 1969), aminocarb has an appreciable percutaneous toxicity. As reported in Table 5-1, however, the dermal LD_{50} values show a wide range of variation, presumably reflecting differences in experimental design and in the formulations tested. In all the dermal tests (Table 5-1), the material was applied to the clipped or shaved skin of the back and held in place for 24 h, usually by covering it with adhesive tape. Most of the reported dermal LD_{50}s in rats lie between 200 and 300 mg.kg-BW^{-1}, but the liquid formulation with 34% aminocarb (the composition was otherwise not specified) appears to be less toxic by the dermal route than alcohol or xylene solutions of aminocarb. The spray concentrate (test no. 29), which has an aromatic petroleum distillate base, yielded the lowest dermal LD_{50}. The dry 50% wettable powder (test no. 31) appeared to be the least dangerous preparation on the skin, but in a later study (DuBois et al. undated) an 80% wettable powder in aqueous suspension yielded a dermal LD_{50} of 250 mg-AI.kg-BW^{-1}. (The later study was not included in Table 5-1 because the number and sex of the rats employed were not specified in the original report.)

In none of the studies of Table 5-1 is there a clear sex difference in the acute toxicity of aminocarb (cf., tests no. 2 and 3, 7 and 8, 9 and 10, 15 and 16, 23 and 24, 32 and 33, 34 and 35). In a few of the tests (cf. 11 and 13, 12 and 14, 19 and 20), there is a weak tendency for the male rat to be slightly more tolerant than the female.

5.5.2 ACUTE TOXICITY IN OTHER LABORATORY ANIMALS

Acute LD_{50} values in other animal species are summarized in Table 5-2. The mouse is more susceptible than the rat to the acute toxicity of intraperitoneal and dermal aminocarb. The same distinction has been noted in inhalation studies (Dilley and Doull 1962; DuBois 1968). Surprisingly, no oral LD_{50} determination in the mouse was located. Guinea pigs and adult hens appear to be somewhat more tolerant to aminocarb than rats. Only petroleum-based formulations have been tested on rabbit skin. They yielded LD_{50} estimates of about 200 mg-AI.kg-BW^{-1} when held on shaved skin for 24 h. It appeared to make little difference whether or not the skin was first abraded with a stiff brush (Crawford and Anderson 1972a).

5.5.3 ACUTE INHALATION STUDIES IN MICE AND RATS

Table 5-3 summarizes available reports. In all but one of these studies, aminocarb in solution was dispersed by aerosolization into the test chamber, and pesticide concentrations were based on analysis of air samples withdrawn from these chambers. In two studies (Mobay Chemical Corporation 1961, 1966) no attempt was made to characterize the aerosol. The droplet size in two other investigations (Dilley and Doull 1962; DuBois 1968) averaged about 2 μm in diameter;

Table 5-2. Acute toxicity of aminocarb in miscellaneous laboratory animals.

Animal	No. Animals	Sex	Route	LD_{50} mg-AI.kg-Bw^{-1}	95% Confidence Limits	Formulation (as stated)	Vehicle (Diluent)	Reference
Mice	40[α]	M	i.p.	8		Bayer 44646	20% ethanol, 80% propylene glycol	DuBois and Raymund (1962b)
Mice	35[α]	F	i.p.	9		Bayer 44646	"	"
	--[β]	F	i.p.	7-10		Bayer 44646	corn oil	"
	--[γ]	F	i.p.	4.7		Matacil	0.1 mL dimethyl sulphoxide	Baron et al. (1964)
	--[γ]	F	dermal	31		Matacil	"	Abdel-Wahab and Casida (1967)
Guinea pigs	30[δ]	M	oral	60		Bayer 44646	20% ethanol, 80% propylene glycol	DuBois and Raymund (1962b)
	34[δ]	M	i.p.	30		Bayer 44646	"	"
Chickens	12[ε]	F	oral	75		Bayer 44646	"	DuBois (1962)
	40[ε]	F	oral	73.7	54-100	Technical (99%)	polyethylene glycol	Kruckenburg (1978)
Rabbits	8[ζ]	M	dermal[η]	203[θ]		Matacil 1.4 OSC (17.4% AI)	undiluted	Crawford and Anderson (1972a)
	8[ζ]	F	dermal[η]	203[θ]		"	"	"
	8[ζ]	M	dermal[η]	180[θ]		"	"	Nelson and Burke (1977a)
	8[ζ]	F	dermal[η]	160[θ]		"	"	"
	4[ζ]	M	dermal[η]	232[θ]	841-1682	Matacil 1.8-585 (19.5% AI)	"	Nelson (1978g)
	4[ζ]	F	dermal[η]	164[θ]	595-1190	"	"	"

[α] Carworth Farms.

[β] Dierolf Farms.

[γ] Berkeley Pacific Laboratories.

[δ] Adults (500-700 g).

[ε] Leghorn adults.

[ζ] New Zealand white rabbits of over 2 kg body weight.

[η] Single application on shaved back, with or without local abrasion with a stiff brush, covered and maintained for 24 hours.

[θ] Derived from the original report.

Table 5-3. Acute inhalation toxicity of aminocarb in mice and rats.

Test No.	Animal	No. Animals	Sex	LC_{50} $\mu g\text{-}AI.L^{-1}$	Exposure period (h)	Lowest test concentration causing deaths ($\mu g.L^{-1}$)	Formulation	AI (%)	Diluent (vehicle)	Reference
1	Rats	40[α]	M	100 1000	4	100	Technical	~100	5% ethanol + Lutrol 9	Mobay Chemical Corp. (1961)
2	Rats	80[α]	M	200	4	153	Heiss A363	~100	alcohol + Lutrol (1:1)	Mobay Chemical Corp. (1966)
3	Rats	80[α]	F	200	4	156	Heiss A363	~100	alcohol + Lutrol (1:1)	Mobay Chemical Corp. (1966)
4	Rats	40[β]	F	100	1	76	Technical	~100	95% ethanol	Dilley and Doull (1962)
5	Mice	60[γ]	F	68	1	58	Technical	~100	95% ethanol	Dilley and Doull (1962)
6	Rats	80[α]	-	>240 <1460	1	240	Matacil 5080A (dust)	~80	none	Kimmerle (1964)
7	Mice	40[α]	-	>240	1	96	Matacil 5080A (dust)	~80	none	Kimmerle (1964)
8	Rats	40[δ]	M	420[ζ] (338-521)	1	334	Matacil 1.8-585	19.9	undiluted	Nelson (1978h)
9	Rats	40[δ]	F	440[ζ] (372-519)	1	334	Matacil 1.8-585	19.9	undiluted	Nelson (1978h)
10	Rats	42[δ]	F	1050	0.5	969	Liquid formula[η]	34	undiluted	DuBois (1968)
11	Mice	50[γ]	F	610	0.5	476	Liquid formula[η]	34	undiluted	DuBois (1968)

[α] Strain unspecified.

[β] Sprague-Dawley.

[γ] Carworth Farms.

[δ] Sprague-Dawley derived (Holtzman).

[ζ] Values computed from data in original report, which specified only micrograms of formulations.

[η] Although not stated in the original report, this formulation may contain 66% N-methyl-2-pyrrolidone.

half the droplets had diameters between 1 and 3 μm. In the most recent study (Nelson 1978h), which employed an oil-base formulation, 93 to 95% of the aerosolized droplets were said to have diameters <1 μm. The exception was a study by Kimmerle (1964) in which a dry formulation of aminocarb was dispersed as an air-dust mixture; the particle size was not measured.

In accord with toxicity data based on other routes of administration (see above), mice proved to be more susceptible than rats to aminocarb aerosols (cf. tests no. 4 and 5, and 10 and 11 in Table 5-3). As expected, the aminocarb LC_{50} in air is less in a 1-h exposure than in a 30-min exposure (cf. tests no. 9 and 10). In the experiments of Dilley and Doull (1962) (tests no. 4 and 5), the LC_{50} values appear to be unaccountably lower than in the other studies listed, perhaps because of the high ethanol concentration employed. However, rats who inhaled a control ethanol aerosol displayed only mild drowsiness (Dilley and Doull 1962). Variations in LC_{50} like those in Table 5-3 are not unusual in the literature. Some of the non-surviving animals died during the exposure period (25 to 30% in Dilley and Doull's trials), but most died during a period of several hours after leaving the exposure chamber (Mobay Chemical Corporation 1961; DuBois 1968; Nelson 1978h).

5.5.4 OCULAR ABSORPTION AND EYE IRRITATION

In addition to studies of the percutaneous toxicity of aminocarb, attempts have been made to assess the hazard of aminocarb formulations in the eye. During a 3 d study on four dogs which received repeated intraconjunctival installations of an 80% wettable powder of aminocarb, marked miosis was observed in all animals shortly after the compound was applied (Nelson 1965). After receiving 2 $mg.kg\text{-}BW^{-1}$ (divided between the 2 eyes) twice daily for 2 d, one of the dogs showed muscle twitching and subsequent vomiting. These observations suggest that absorption from the eye (or from the nasal mucosa onto which tears drain through the nasolacrymal duct) can lead to systemic poisoning. Nelson's (1965) conclusion, that the eye is a relatively inefficient route of absorption for the wettable powder, appears to be inadequately supported by the data presented.

Although no irritation was observed in the eyes of dogs which received 2 $mg.kg\text{-}BW^{-1}$ of an 80% wettable powder of aminocarb in the conjunctival sac, as often as 6 times daily (Nelson 1965), oil-based aminocarb formulations have proven to be irritating in rabbit eyes and on rabbit skin. Nine New Zealand rabbits each received 0.1 mL of Matacil 1.4 OSC (which is said to be 17.4% aminocarb). The treated eyes of 3 rabbits were washed with water 45 seconds after administration of the pesticide; eyes of other rabbits were not further treated. No corneal lesions or signs of iritis were found in any of the rabbits, but all of them showed conjunctival irritation with varying degrees of chemosis and discharge (Nelson and Burke 1977b). In both washed and

unwashed eyes, these signs persisted for 4 d but had disappeared by the 7th day. Matacil 1.8-585 was evaluated in a similar Draize-type test performed on 9 New Zealand white rabbits (Nelson 1978i). Again, erythema and mild to moderate chemosis were observed for 4 days after treatment but not after 7 d, except for 1 female in which discharge and conjunctival edema persisted for 14 d. Although these two aminocarb formulations can be properly classified as mild-to-moderate reversible ocular irritants, no controls were performed with the vehicle itself (nonyl phenol and oil?), and so the role of aminocarb in these reactions is unknown. Surprisingly, no miosis or other signs of systemic poisoning were reported in these rabbits (Nelson and Burke 1977b; Nelson 1978i).

5.5.5 SKIN IRRITATION

Two oil-based formulations have been tested for primary irritancy on clipped rabbit skin, without local abrasion. Nelson and Burke (1977a,b) tested "Matacil 1.4 OSC " and Nelson (1978i) tested "Matacil 1.8-585." In both cases 0.5 mL of formulation was applied and held at each of two test sites under a 2.5-cm (1-inch) gauze patch for 24 h. Erythema and local edema of the skin were observed after 24 h and again after 72 h. Both formulations were judged to be moderate dermal irritants.

Because no controls were performed with the nonyl phenol base alone, the role of aminocarb in these dermal reactions cannot be assessed. It seems unlikely, however, that aminocarb itself is a skin irritant. For example, no skin reactions were described in Sprague-Dawley rats on whose clipped and abraded skin an 80% wettable powder was applied at dose levels of 30 and 60 mg.kg-BW^{-1}, 5 d per week, for a period of 3 weeks (DuBois *et al.* undated). The higher dose level was sufficient to cause systemic reactions consisting of mild cholinergic symptoms.

One report (Mobay Chemical Corporation 1961) states that no primary skin damage was observed in 6 male persons on whose lower arm "the chemical was fixed ... for 24 hours." It is not clear what formulation of Bayer 44646 was used in this brief clinical study.

5.5.6 POTENTIATION OF ACUTE TOXICITY IN RATS

In view of the widely held belief that tissue cholinesterase inhibition is the basis of the toxicity and lethality of aminocarb and of other anticholinesterase pesticides, one expects additional deaths when two or more of these agents are administered simultaneously. DuBois and Raymund (1962c) injected adult female rats intraperitoneally with a dose equal to half the LD_{50} of aminocarb and, at the same time, a dose equal to half the LD_{50} of each of 15 other anticholinesterase

pesticides (all of organophosphorus type). In each case less than half the test animals died. While the results do not demonstrate "less than additive mortality", as claimed by the investigators, the data do demonstrate an absence of potentiation. It would be imprudent, however, to conclude that positive toxic interactions do not occur under some dosage regimens. The limited data base available does not exclude the possibility that aminocarb is less hazardous to a normal test subject than to one with a recent prior exposure to any anticholinesterase agent.

5.5.7 ACUTE TOXICITY OF AMINOCARB METABOLITES

Studies on the anticholinesterase activity and acute toxicity of aminocarb metabolites are summarized in Table 5-4. For these investigations the metabolites were either synthesized de novo (e.g. Abdel-Wahab and Casida 1967; Thomas and Kimmerle 1974) or they were isolated from liver microsomal incubates (e.g. Oonnithan and Casida 1968).

While metabolic alterations in toxic molecules generally serve to reduce their lethality, many exceptions are known in which initial enzymatic steps generate substances that are as toxic or even more toxic than the parent compound. That this is the situation with aminocarb is amply demonstrated by the data in Table 5-4. Although the two formamide metabolites (MFC and FC) are somewhat less active than aminocarb (A), the products of demethylation of the ring amino group (MAA and AA) are as toxic or more toxic than the parent pesticide. Only the ester hydrolysis product of aminocarb (C) is devcid of demonstrable lethality in rats and mice. In general, the data in Table 5-4 show a high correlation between acute toxicity in laboratory rodents and anticholinesterase activity (even though the two in vitro bioassay systems used human plasma that contains only pseudocholinesterase). This concordance suggests that the acute toxicity of these metabolites is due to their ability to inhibit cholinesterase enzymes in vivo.

Little is known about the biological activities of the other aminocarb metabolites (Figure 2-6), but HMA is said to be as potent as aminocarb in inhibiting plasma cholinesterase (Oonnithan and Casida 1968). Almost certainly the various ester hydrolysis products (phenols) and their glucuronides or other conjugation products lack the capacity to inhibit cholinesterase and are devoid of significant acute toxicity.

No reports were located in which the LD_{50} of aminocarb was measured in rats (or other mammals) pretreated with either an inducer of liver microsomal enzymes (such as phenobarbital) or an inhibitor of these metabolizing enzymes (such as SKF 525A). In the absence of this information, it is impossible to be certain about the roles, if any, of aminocarb metabolites in the acute toxic reactions observed in animals given the parent pesticide.

Table 5-4. Acute toxicity and anticholinesterase activity of aminocarb and metabolites.

Compound	Anticholinesterase activity MDL[α] (µg)	pI_{50}[β] human plasma	pI_{50}[β] housefly heads	Animal	No.	Sex	Route	LD_{50} mg.kg^{-1}	95% Confidence limits	Reference for LD_{50}
A	1.0	5.0	6.4	Rats			oral	20-30		viz. Table 5-1
				Mice			i.p.	5-9		viz. Table 5-2
				Mice		F	dermal[γ]	31		Abdel-Wahab and Casida (1967)
C	?			Rats	8	F	oral[δ]	>1000		DuBois (1963)
				Rats	7	M	dermal[ε]	>1000		DuBois (1963)
MFC	1.0	4.8	5.7	Rats	60	F	oral[ζ]	103	(89-119)	Thomas and Kimmerle (1974)
				Mice		F	i.p.[η]	21		Abdel-Wahab and Casida (1967)
				Mice		F	dermal[γ]	>500		"
MAA	0.1	5.5	6.4	Rats	60	F	oral[ζ]	27.8	(23-34)	Thomas and Kimmerle (1974)
				Mice		F	i.p.[η]	3.0		Abdel-Wahab and Casida (1967)
				Mice		F	dermal[γ]	52		"
FC	1.0	4.7	5.7	Rats	50	F	oral[ζ]	40.1	(34-47.5)	Thomas and Kimmerle (1974)
				Mice		F	i.p.[η]	13		Abdel-Wahab and Casida (1967)
				Mice	-	F	dermal[γ]	500		"
AA	0.1	5.6	6.6	Rats	60	F	oral[ζ]	18.3	(16-21)	Thomas and Kimmerle (1974)
				Mice		F	i.p.[η]	1.6		Abdel-Wahab and Casida (1967)
				Mice		F	dermal[γ]	17		"

[α] The minimum detectable limit in a crude cholinesterase assay system involving human plasma, according to the method and data of Oonnithan and Casida (1966, 1968). The numerals are approximately inversely proportional to the anticholinesterase activity relative to that of aminocarb.

[β] The negative logarithm of the molar concentration required to effect 50% inhibition of the enzyme, based on the volume of enzyme and inhibitor solution prior to the addition of substrate, according to Abdel-Wahab and Casida (1967).

[γ] Based on the 24-h mortality after application of 20 µL of a dimethylsulfoxide solution to the shaved back, with confinement of the mouse for the first 6 hours.

[δ] Dissolved in 20% ethanol-80% propylene glycol and administered to Sprague-Dawley rats by gavage.

[ε] Dissolved in xylene and applied to skin of Sprague-Dawley rats.

[ζ] Emulsified in water and Emulsifier W233 and administered to Wistar rats by gavage in a volume of 1 mL per 100 g-body weight.

[η] Injections involved 0.1 mL dimethylsulfoxide, containing the test compound, per 10 g-body weight.

5.5.8 ACUTE TOXICITY OF ADJUVANTS

5.5.8.1 Nonyl Phenol

Mean lethal doses (LD_{50}) for oral and dermal exposure are summarized in Table 5-5. The purity of nonyl phenol was not indicated in the studies and also, in many cases, it was not stated whether a dilution was used. However, the LD_{50} values for oral exposure appear to range from 400 to 3389 $mg.kg\text{-}BW^{-1}$ for rats. For the lower LD_{50} values, undiluted nonyl phenol appears to have been used. The oral LD_{50} value for mice ranges from 910 to 1665 $mg.kg\text{-}BW^{-1}$.

Dermal LD_{50} values by 24 h continuous contact with rabbit skin are approximately 2 $mL.kg\text{-}BW^{-1}$ (Smyth et al. 1962, 1969).

In an acute inhalation test in which rats were exposed to an atmosphere saturated with nonyl phenol vapors at room temperature, no deaths resulted after a 4 h exposure (Smyth et al. 1969). Assuming that room temperature was 25°C, the vapor pressure of nonyl phenol would be 10 mm (1.33 kPa). The maximum vapor concentration to which the rats were exposed would be 1.32×10^{4} $mg.L^{-1}$.

In another study (Jefferson Chemical Company Inc. 1964) an 8 h exposure to a near-saturated atmosphere at room temperature caused no fatalities among a group of six rats. Similarly, another group survived a 4 h exposure to mist generated from nonyl phenol heated at 170°C. However, an 8 h exposure to the mist killed two of six rats.

Prolonged contact with the skin produces local burns, irritation, edema and eschar formation. Hence, nonyl phenol may be classed as a mild-to-moderate skin irritant (Rohm and Haas Co. 1975). An irritation study resulted in necrosis when 0.01 mL of undiluted nonyl phenol was applied to the uncovered rabbit belly (Smyth et al. 1962, 1969).

A sensitization study was conducted with male guinea pigs of the Hartley strain. The study used 0.05 mL and 0.1 mL of a 0.1% dilution of nonyl phenol in peanut oil, representing 5.3×10^{-5} mL and 1.1×10^{-4} mL of nonyl phenol respectively. The sensitization response was determined to be moderate while the sensitization potential was severe (Gaworski et al. 1979).

Tests on rabbits show that nonyl phenol is a severe and rapid-acting irritant to the eyes. Even solutions as dilute as 1% cause severe injury (Rohm and Haas Co.1975). Severe burns in rabbit eyes were reported following the administration of 0.5 mL of a 1% solution of nonyl phenol (Smyth 1962, 1969). This represents approximately 5.3×10^{-4} mL of nonyl phenol.

Table 5-5. Acute toxicity of nonyl phenol.

Route	Animal (Sex)	Diluent	LD_{50} (95% confidence intervals) $mg.kg\text{-}BW^{-1}$	Reference
Oral	Rats (M)	Undiluted	600 (400-800)	Jefferson Chemical Co. Inc. (1964)
Oral	Rats	Not stated[a]	400-1400	Hart Chemical Ltd. (1978)
Oral	Rats	Not stated[a]	1620	Dorigan et al. (1976)
Oral	Rats (M)	Dissolved in corn oil	2462 (1788-3389)	Gaworski et al. (1979)
Oral	Rats	Undiluted	1.62 (1.06-2.50) $mL.kg^{-1}$	Smyth et al. (1969)
Oral	Mice	Dissolved in corn oil	1231 (910-1665)	Gaworski et al. (1979)
Dermal	Rabbits	Undiluted (24-h contact)	21 $mL.kg^{-1}$	Jefferson Chemical Co. Inc. (1964)
Dermal	Rabbits	Not stated[a] (24-h contact)	2.14 (1.52-2.99) $mL.kg^{-1}$	Smyth et al. (1969) Smyth et al. (1962)

[a] Nonyl phenol was probably undiluted.

5.5.8.2 Diluent 585

The polynuclear aromatics which have been found in some crude oils have been shown to be carcinogenic in test animals. However, the polynuclear aromatic content of distilled oils is dependent upon the distillation temperature and source. It is therefore essential to select a distillation temperature below which these aromatics would not be carried over into the end product. The desired temperatur for oils is 580°F (304.4°C) with a maximum allowable distillation temperature of 585°F (307.2°C) (Agriculture Canada 1978). The selection of a virgin distillate prevents the formation of double bonds in the carbon chain which may result in greater reactivity.

The median lethal dose (LD_{50}) for oral exposure to diesel fuel (No. 2 fuel oil) is greater than 8 $g.kg^{-1}$ in rats, while the dermal LD_{50} value is greater than 4 $g.kg^{-1}$ (Shell Chemical of Canada 1981).

Petroleum solvents of this class have been described as being moderately toxic by the oral and inhalation routes. If aspirated however, severe lung irritation occurs and pulmonary edema rapidly develops. Later signs of bronchopneumonia and pneumonitis may result. Skin and eye irritation have been described as moderate (Shell Chemical of Canada undated).

5.6 SUBACUTE TOXICITY

5.6.1 SUBACUTE TOXICITY IN RATS

Subacute toxicity usually refers to the consequences of multiple dosing with an intoxicant at frequent intervals (usually daily) for several days up to several months. Three relevant investigations with aminocarb have been reported, involving the intraperitoneal, oral and dermal routes of administration, respectively.

Sprague-Dawley rats received daily intraperitoneal injections of aminocarb (Bayer 44646) dissolved in 20% ethanol and 80% propylene glycol; the volume injected was equivalent to 0.1% of the body weight (DuBois and Kinoshita 1962). Five female rats were used at each of 5 daily dose levels (0, 2, 4, 8, and 10 $mg.kg\text{-}BW^{-1}$). At 10 $mg.kg\text{-}BW^{-1}$, all 5 rats were dead within 10 d, but at 8 $mg.kg\text{-}BW^{-1}$, only 1 rat died within the 60-d test period. Since the single-dose acute LD_{50} of this formulation is only 13 $mg.kg\text{-}BW^{-1}$ (DuBois and Raymund 1962a), these observations demonstrate the ability of most rats to tolerate about two-thirds of the mean lethal dose given every day for 60 days. At least in terms of mortality, aminocarb is not a cumulative poison in rats. However, daily doses of 4 $mg.kg\text{-}BW^{-1}$ and above were sufficient to prevent any weight gain. No histopathology was reported in this study.

Weanling Sprague-Dawley rats (84 males and 84 females) were fed a wettable powder (concentration of aminocarb not specified but

presumably 50%) mixed with the chow diet, for periods up to 4 months (Root et al. 1963). The dietary levels employed were 0, 5, 10, 50, 100 and 200 mg.kg-diet^{-1} "of the insecticide" (meaning active ingredient according to Misener (1981)). Because no cholinesterase inhibition could be demonstrated at 50 mg.kg-diet^{-1} or lower after 4 months, or at 100 and 200 mg.kg-diet^{-1} after 3 weeks, the pesticide level was raised in the two latter groups to 400 and 800 mg.kg-diet^{-1}, respectively, for the remaining 14 weeks of the feeding study. None of the animals died during the test, and although many of them were hyperirritable, none exhibited cholinergic symptoms or other clear-cut toxic signs and symptoms. No appreciable inhibition of growth occurred at dietary levels as high as 200 mg.kg-diet^{-1}, but weight gains were impaired moderately at 400 and 800 mg.kg-diet^{-1}, despite the fact that the intake of food was well sustained. As noted later, serum cholinesterase was inhibited at the two highest dietary levels but not significantly at 200 mg.kg-diet^{-1}. Organs were removed for microscopic examination when animals were sacrificed at the end of the feeding period, but no significant alterations in organ weight or other gross pathological lesions were detected.

Rats can also tolerate repeated daily doses equivalent to one-tenth and one-fifth of the dermal LD_{50} applied to the skin 5 days per week for 3 weeks without mortality, inhibition of growth rate, deviations in white and red blood cell counts or in hemoglobin levels, abnormalities in organ weight or in histopathology (DuBois et al. undated). In this study the formulation used was an 80% wettable powder suspended in water and applied to intact or abraded skin at daily doses of 30 and 60 mg.kg-BW^{-1}. (The acute single-dose dermal LD_{50} of this preparation is approximately 300 mg.kg-BW^{-1}, equivalent to 240 mg.kg-BW^{-1} of active ingredient.) At least at the higher of the two daily dose levels (60 mg.kg-BW^{-1}), some percutaneous absorption occurred as indicated by the appearance of mild cholinergic signs. Apparently, rats with abraded skin responded similarly to those with unabraded skin.

5.6.2 SUBACUTE TOXICITY IN CATS AND DOGS

For 10 consecutive days a cat tolerated daily doses of 5 mg.kg-BW^{-1} of aminocarb administered as a 0.25% emulsion in an unspecified oil (Mobay Chemical Corporation 1961). It exhibited a temporary loss of appetite, weight loss and salivation, but no other toxic signs were observed during the test or during a 3 week post-test period. At 10 mg.kg-BW^{-1} administered orally, 2 other cats promptly displayed clinical signs of cholinesterase inhibition and died on the third or fourth day.

In a 12-week study in dogs (8 male and 8 female adult pedigree beagles) involving dietary levels of 200, 400 and 800 mg.kg-diet^{-1} aminocarb (Bayer 44646), various signs of cholinergic stimulation were

encountered but no deaths occurred (Doull and Root 1963). The signs, which consisted of vomiting, ataxia and salivation, occurred in both sexes fed the 300 mg.kg-diet^{-1} but only in female dogs at 400 and 200 mg.kg-diet^{-1}. For the most part the signs were limited to the period immediately after eating and were minimal or absent during the remainder of the day. In spite of this clear-cut clinical evidence, no significant inhibition of serum or red cell cholinesterase was detected in any of these animals by manometric or radiometric assay techniques.

5.6.3 SUBACUTE TOXICITY OF ADJUVANTS

Subacute toxicity studies could not be found for nonyl phenol or diluent 585.

5.7 CHRONIC TOXICITY

Over the past decade or more considerable effort has been expended to understand the etiology of human cancer. Various chemicals, including pesticides, have been implicated as potential causative agents. The term chemical carcinogenesis means "the induction or enhancement of neoplasia by chemicals. The terms tumourigen, oncogen and blastomogen have all been used synonymously with carcinogen although occasionally tumourigen has been used specifically to denote the induction of benign tumours" (IARC 1976).

Until the mechanisms of the carcinogenic response are understood it will not be possible to resolve the controversy amongst scientists as to whether exposure to any level of a carcinogen is potentially capable of inducing a tumor or whether a certain threshold level must be attained before the process is initiated. Some compounds may fall into one of these categories and some into the other. There are also compounds which themselves do not cause cancer but promote the carcinogenic effects of other compounds.

Animal testing appears to have merit in the qualitative assessment of the potential carcinogenicity of a chemical, but this does not necessarily mean that a compound which induces cancer in animals will do so in man under the conditions of human exposure or vice versa. Not only are these tests difficult to conduct but also the interpretation and extrapolation of the data to humans are extremely complex. Eventual extrapolation of the animal data to quantify the risk to humans may be facilitated through the use of mathematical models. Although there is frequently great debate over the application of these models, useful information may sometimes result.

In addition to ascertaining whether a compound is a carcinogen, it is desirable to know what other toxic effects might occur following repeated exposure over the lifetime of the animal. Although

there are differences in the way each of the studies would be designed to test for these two categories of effects, it is certainly possible that they can be combined into one study.

5.7.1 CHRONIC FEEDING STUDIES IN RATS

In mammals, there have been two chronic feeding studies completed on aminocarb and a third study is nearing completion. Groups of 24 male and 24 female weanling (80-120 g-BW) Sprague-Dawley rats were fed 0, 100, 200, 400 or 800 mg.kg-diet^{-1}.d^{-1} which is approximately 0, 5, 10, 20 or 40 mg.kg-BW^{-1}.d^{-1} of technical (98.3%) aminocarb in Rockland rat diet for up to 84 weeks (Doull et al. 1967). Diets were prepared biweekly or more often; mortality was checked daily and food intake was calculated biweekly. Five males and five females per group were used for blood and tissue cholinesterase determinations by the manometric method. Tissues from 5 males and 5 females per group, killed at about 68 or 84 weeks, were examined histologically.

Food intake was stated to be slightly depressed during the "first few weeks" in the 400 and 800 mg.kg-diet^{-1} male groups only. Weight gain was depressed at 800 mg.kg-diet^{-1} in both males and females and at 400 mg.kg-diet^{-1} in males only during the first year of the study. There was a decline in body weight and increase in mortality by 68 weeks in the male control group that was unusual and may indicate an infection in that group. The treatment did not appear to have a significant effect on survival in the females (30-40% at 84 weeks). It is difficult to comment on the males because of the unusual mortality in the control group. However, the survival rate in the 800 and 400 mg.kg-diet^{-1} groups was approximately 20 to 40% as well.

The mean serum, red blood cell and brain cholinesterase levels, determined after 84 weeks, were not significantly different from those of the control groups. There was a tendency to reduced cholinesterase levels in submaxillary glands at 800 mg.kg-diet^{-1} (ca 20%).

At the end of the feeding period, 5 males and 5 females from each group were sacrificed with ether, then were exsanguinated and autopsied. The following organs and tissues were examined and removed: brain, liver, thymus, kidneys, urinary bladder, spleen, heart, lungs, testes, ovaries, thyroid, parathyroid, adrenal glands, duodenum, pancreas, stomach, mesenteric lymph nodes, jejunum, ileum, colon and bone marrow. The tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned, mounted and stained with hematoxylin and eosin.

In the lung tissue, interstitial and/or peribronchial lymphocytes appeared in both control and treated groups. Occasional respiratory infections (purulent reactions) were observed. In the

heart, a mild vacuolar and interstitial reaction was observed in male and female rats of the 800 mg.kg-diet^{-1} groups and males dosed at 400 mg.kg-diet^{-1}. The heart tissue of rats treated with doses less than 400 mg.kg-diet^{-1}, and of control rats were unaffected. One male in the 800 mg.kg-diet^{-1} group and two in the 400 mg.kg-diet^{-1} group had a reduction in spermatogenesis, a not uncommon finding in old rats. The keratinization of the uterine epithelium found in one animal from each of the treated groups is not an uncommon finding in old rats. Adrenal cysts were seen in the control and most of the treated groups, however no correlation could be made between this finding and treatment. Vacuolar and fatty changes were observed in male and female rats treated with 200 mg.kg-diet^{-1} or more. In the kidney, eosinophilic casts were observed in control and all tests groups. Overall, it would appear that the no-effect level was 100 mg.kg-diet^{-1} (~ 5 mg.kg-BW^{-1}). However, the small number of rats examined does not allow that to be decided with certainty. This study does not meet the requirements of presently accepted testing protocols as a chronic toxicity study or as an oncogenicity study. However, there was no reported incidence of tumor induction.

A study in rats conducted according to more modern standards (Mobay Chemical Corporation 1981) is nearing completion. Groups of male and female rats were fed 0, 25, 150 or 900 mg.kg-diet^{-1} (~ 0, 1.25, 7.5 or 45 mg.kg-BW^{-1}.d^{-1}) of 97.4% pure aminocarb in their diet for up to 24 months. The preliminary results indicate that the test compound did not increase mortality. Food consumption, body-weight gain and blood cholinesterase activity were reduced at the highest dose level. Hematological, blood chemistry, and urinary parameters of control and treated groups appeared to be comparable. There were no overt signs of toxic effects in the treated animals other than the cholinesterase inhibition.

5.7.2 CHRONIC FEEDING STUDIES IN DOGS

Noel et al. (1966) conducted chronic feeding studies in which groups of beagle dogs (4/sex/dose-level) of initial body weight 5.8-9.7 kg, received 0, 2, 4, or 10 mg.kg-BW^{-1}.d^{-1} of 96% pure aminocarb perorally in gelatin capsules, in two equally divided doses 0.5 h after feeding, daily for up to 2 years. The amount of food offered was restricted such that little or no food was left unconsumed. Water was available ad libitum and clinical, hematological, biochemical and urine examinations were performed at regular intervals during the study. Survivors were killed at 24 months, and necropsy and histological examinations were carried out.

One female and one male in the low- and medium-dose groups died of accidental or unknown causes during the study and were replaced on days 71 and 32 respectively; 1 female (not replaced) in the high-dose group died of toxic causes (cholinergic effects) after week 12; 1

female (not replaced) in the low-dose group died on day 706. A number of immediate signs characteristic of cholinergic response (tremors, weakness in limbs, cough, convulsions and vomiting salivation) were seen at 0.5 to 2 h after dosing. No other signs were observed during the first three months, and those that appeared with increased duration of dosing were considered to be generally mild.

The highest dose level (10 mg.kg-BW^{-1}.d^{-1}) had an effect on body weight gain. Plasma and RBC cholinesterase levels, when measured on 5 occasions and sometimes with 2 different methods and/or duplicate determination (ΔpH), were unaffected when tested either just prior to daily dosing or at 0.5 to 1 h after. Since most of the dogs were exhibiting obvious cholinergic signs, the timing of the sampling or the method of analysis may be open to question. It would appear that 2 mg.kg-BW^{-1} would be a likely NOEL for cholinergic effects, not 10 mg.kg-BW^{-1} as suggested in the report. However, the rapid spontaneous recovery of the mild signs at even the highest levels would suggest that aminocarb is not a potent cholinesterase inhibitor. A number of other parameters were measured (including urea, glucose, protein (total, albumin, globulins), alkaline phosphatase, glutamic-pyruvic transaminase, bilirubin and serum isocitrate dehydrogenase) and the NOEL was 10 mg.kg-BW^{-1}.d^{-1}. There were also no significant changes measured in the standard hematological parameters or urinalyses.

At necropsy there were no consistent abnormalities to suggest toxic damage. Some of the animals had tapeworms or roundworms in their gut and some control dogs were obese. Several absolute and relative body weights showed a trend which suggested a treatment effect at 10 mg.kg^{-1}.d^{-1}. Adrenal hypertrophy was seen and the liver increased in weight at the highest dosage. It was stated in the report that the hepatocyte enlargment was due to glycogen infiltration which was considered to be a normal physiological reaction resulting from lengthy feeding of a laboratory diet. However, the results were more pronounced in the highest dose group. Although this study was not designed as an oncogenicity study, there were no reported increased incidences of tumors.

It would appear that the overall NOEL for the study was 2 mg.kg-BW^{-1}.d^{-1} for slight clinical signs (rapidly reversible body tremors) and slight histologic effects (increased incidence of lipofuscin-laden liver in macrophages). Lethal effects can be expected at 10 mg.kg-BW^{-1}.d^{-1}. One female died towards the end of the experiment of "toxic causes", hind limb weakness was observed in 6/8 dogs and 1 animal died after onset of paralysis.

5.7.3 CHRONIC STUDIES ON ADJUVANTS

Chronic studies could not be found for nonyl phenol or diluent 585.

As discussed (Section 5.5.8.2), potentially carcinogenic polynuclear aromatics are unlikely to be present in diluent 585.

5.8 RELATION BETWEEN CHOLINESTERASE INHIBITION AND TOXICITY

Many studies have attempted to establish correlations between inhibition of blood and tissue levels of cholinesterase activity and clinical signs and symptoms of intoxication in exposed animals. The attempts have not been notably successful, and several examples can be cited where no enzyme inhibition was demonstrated in spite of evident cholinergic-type symptoms. For example, cholinesterase activities measured against 4 out of 5 choline esters were essentially the same as control values in the livers and brains of mice having received an intraperitoneal LD_{50} of aminocarb in corn oil (Baron et al. 1964). No inhibition of cholinesterase activity in serum or red cells could be demonstrated by manometric or radiometric assay procedures in dogs fed aminocarb at levels as high as 800 mg.kg-diet^{-1}, perhaps because the blood was drawn just before the feeding periods whereas symptoms were much more pronounced immediately after the feeding (Doull and Root 1963). In rats on dietary levels as high as 800 mg.kg-diet^{-1}, there was no significant inhibition of cholinesterase activity in the brain, submaxillary glands or erythrocytes (Root et al. 1963). The serum enzyme activity, however, was reduced in both male and female rats receiving 800 mg.kg-diet^{-1}, an effect more marked in females than in males. The functional significance, if any, of inhibition of the serum enzymes has not been established.

The common failure to find significant inhibition of cholinesterase in brain and other organs may reflect the highly transient nature of the inhibition. Recovery from enzyme inhibition by several carbamate insecticides has been shown to be surprisingly rapid both in vivo and in vitro (Casida 1963; Wilson et al. 1960). For example, with bovine erythrocytic acetylcholinesterase, the in vitro recovery half-time at pH 7 is 19 min for the methylcarbamylated enzyme and 56 min for the diethylcarbamylated enzyme (Aldridge and Reiner 1972). Various procedural differences may also contribute to inconsistencies in published data. For example, sample dilution is known (Wilson et al. 1960) to promote reversal of enzyme inhibition by speeding the hydrolysis of the carbamylate enzyme. Furthermore, the degree of esterase inhibition varies with the enzyme source, the test substrate (including various choline and noncholine esters), substrate concentration and pH (Baron et al. 1963). Apparently few toxicolgists have determined optimal conditions for their enzyme determinations.

In spite of these difficulties and uncertainties, inhibition of cholinesterase in red cells and in some tissues has been demonstrated in single- and multiple-dose tests. For example, male and female rats were dosed orally with aminocarb dispersed in polyethylene glycol-400 at single doses of 0.5, 2 and 8 mg.kg-BW^{-1} (Nelson 1978c). Blood samples

were taken at 1, 3, 5, 24 h and 7 d after dosing. Even at the highest dose level the inhibition of serum and red-cell cholinesterase was small and somewhat erratic, and enzyme activity had returned essentially to normal 5 h after dosing. With higher doses the results were less equivocal. Nine rats received, by stomach tube, 25 mg.kg-BW^{-1} of aminocarb in oil (Mobay Chemical Corporation 1961). Erythrocyte cholinesterase levels were found to be reduced by about 50% after 3 and 5 h, whereas they had returned to normal at the end of 24 h.

Enzyme inhibition has also been demonstrated after multiple doses. For example, rats were given, by stomach tube, 5 mg.kg-BW^{-1} of aminocarb in oil daily for a period of up to 28 d (Mobay Chemical Corporation 1961). During the dosage regimen, no toxic signs or symptoms were observed, but erythrocyte cholinesterase levels were inhibited to the extent of about 20 to 30% of the controls. Female Sprague-Dawley rats received daily intraperitoneal injections of aminocarb in ethanol-propylene glycol for periods of up to 60 d (DuBois and Kinoshita 1962). Daily doses ranged from 0 to 10 mg.kg-BW^{-1}. All five rats at the highest dose level died within 10 d, but 4 of 5 rats at 8 mg.kg^{-1} survived for the entire test period. At sacrifice after 60 d, the average inhibition of submaxillary gland cholinesterase was 11.4, 23.6 and 34.3% at daily doses of 2, 4 and 8 mg.kg-BW^{-1} respectively. The corresponding inhibition of the serum enzyme was 28.8, 43.5 and 52.7%. In none of the animals was there a demonstrable inhibition of brain cholinesterase.

In fact, no investigator appears to have reported a significant inhibition of brain cholinesterase by aminocarb in vivo. Although, no doubt, some carbamate insecticides penetrate the mammalian brain in toxicologically significant amounts (e.g. Bagdon and DuBois 1956; Carpenter et al. 1961), it is possible that aminocarb does not cross the mammalian blood-brain barrier in sufficient amounts to inhibit brain cholinesterase. A corollary of this inference is that the toxic signs and symptoms and mode of death must be sought in terms of peripheral mechanisms. The issue, however, cannot be resolved without further experimentation.

In spite of the difficulties enumerated above in demonstrating cholinesterase inhibitors, there are no valid reasons to doubt that this inhibition, in peripheral tissues if not in the central nervous system, is the critical lesion responsible for the toxicity and lethality of aminocarb.

5.9 SPECIAL TOXICITY STUDIES

5.9.1 REPRODUCTION STUDIES

A reproduction study is designed to assess the potential effects of a chemical on the parental generation with regard to mating,

conception, pregnancy and lactation, and on the growth and development of some of the offspring from conception through maturity for multiple generations. Dosing of the parental generation (F_0) should commence shortly after weaning and acclimation and before the animals are 6 weeks old. The dosing should continue until all the offspring (F_1) have been weaned. The dosing of the F_1 generation should begin immediately after the animals are weaned and continue throughout their breeding period until their offspring (F_2 generation) have been weaned. This process is then repeated to give subsequent generations as desired.

This type of schedule ensures that the F_0 generation is exposed to the chemical from shortly after weaning through to maturity. The period of dosing prior to mating must cover the time required for at least one spermatogenic cycle in males and two estrous cycles in females. The second generation (F_1) would potentially be exposed to the chemical in utero and through nursing. Upon separation of the young from the mother, the test diet is fed to the young so that there is no break in exposure to the chemical. Possible effects on their reproductive capacity would be determined when they were bred. Subsequently, the F_2 generation would be exposed in utero and through nursing to pick up any effects that might not be manifest in the first 2 generations. Experience has shown that little additional information is gained in the F_3 generation, and newer studies tend to include 2 litters (a and b) in 2 generations.

The toxic effects of aminocarb and its effects on reproduction with regard to three parental generations of rats (F_0, F_{1b}, F_{2b}), each parental generation producing two litters (F_{1a}, F_{1b}, F_{2a}, F_{2b}, F_{3a}, F_{3b}), was assessed by Palmer and Fletcher (1966). The test compound was administered at levels of 0, 100, 200 and 800 mg.kg-diet^{-1}. The following parameters were recorded in the parental animals: signs of toxicity, mortality, body weight until pairing and conception rate. In males only, food consumption was spot-checked during the terminal weeks of the experiment. For all litters, the litter size, still-birth incidence, litter and mean pup weight at birth, litter size at weaning, litter and mean pup weight at weaning, pup mortality during lactation and abnormal fetuses were recorded.

When aminocarb was administered at 800 mg.kg-diet^{-1}, adjective signs of hypersensitivity were observed in both sexes. In addition, body weight gain was retarded in all male parental rats and in female parental rats in the F_0 and F_{2b} generations. A similar but less severe growth retardation was noted at 200 mg.kg-diet^{-1} in male parental rats of the F_{1b} and F_{2b} generations. No effect on growth was observed at 100 mg.kg-diet^{-1}. Food consumption, although only spot-checked in male rats of the F_{2b} generation during the last 7 weeks of the experiment, showed a dose-dependant decrease at 200 and 800 mg.kg-diet^{-1}. The decreased food intake showed a close relationship to the observed growth retardation in the male animals. Parental mortality did not show any compound or dose-related correlation. Neither did conception rates

although these varied considerably (20-100%). In all matings of the control group, conception rates were lower than the conception rate at 800 mg.kg-diet^{-1}.

The data on litters show no compound related effects on mean pup weight at birth, pup mortality (which is frequently high) or incidence of abnormal offspring. However, at 800 mg.kg-diet^{-1}, F_{1a} litters and all offspring resulting from the F_{1b} and F_{2b} parental generations showed a slight reduction in litter weight which was statistically significant only in the F_{3b} litters. In parallel with this observation, litter size in the group receiving 800 mg.kg-diet^{-1} also showed a tendency to be reduced in the offspring of F_{1b} and F_{2b} parents. Again, a statistically significant reduction was only noted in the F_{3b} litters. The litter size at weaning was reduced at 800 mg.kg-diet^{-1} in offspring of F_{2b} matings. However, since the percentage loss of offspring through weaning in control groups is comparable to that at 800 mg.kg-diet^{-1}, this does not appear to be compound related. The loss of whole litters during the rearing period varied considerably and seems not to be affected by treatment. Mean pup weights at birth were comparable in all generations and groups, but a reduction of mean pup weight at weaning was found in all generations treated with 800 mg.kg-diet^{-1}. A similar tendancy was noted in F_{1a}, F_{1b} and F_{2a} offspring at 200 mg.kg-diet^{-1}. Although not statistically significant, this reduction was regarded as an early manifestation of toxicity.

Histopathologic examinations were done on some organs from 10 male and 10 female rats from the control and high-dose level groups of the F_{3b} litters at 21 d. This examination was limited to 13 organs and tissues and did not include the brain. The reporting was limited to observed changes in tissue morphology. The data were not indicative of a treatment effect.

Additional data on estrous cycle and mating performance were provided in the interim report of the parent generation (F_0). The length of the estrous cycle prior to the first mating was not affected by treatment. Observation of the mating performance showed a low copulation frequency in the low-dose group. Because the intermediate- and high-dose groups were comparable in this respect to the controls, the reduced mating rate was not considered to be related to treatment.

From the results of this study, under the experimental conditions pertaining, it can be concluded that aminocarb fed to 3 generations of rats at 800 mg.kg-diet^{-1} resulted in:

(a) hypersensitivity as assessed subjectively in all animals;

(b) growth retardation in all male parental generation rats and in the F_0 and F_{2b} female parental rats during the premating period;

(c) reduction of food consumption in male rats (spot-checked over the last 7 weeks of the F_{2b} generation);

In addition, there was:

(d) a tendency to reduced pup weights at weaning in all generations;

(e) a tendency to reduced litter size in F_{2a}, F_{2b}, F_{3a} and F_{3b} litters, which attained statistical significance in F_{3b} litters;

(f) a tendency to reduced birth weight of litters in F_{1a}, F_{2a}, F_{3a} and F_{3b} litters, which attained statistical significance in F_{3b} litters.

Further studies are in progress (Howard 1982) which should clarify the significance of these trends.

At a dietary level of 200 $mg.kg^{-1}$, aminocarb caused growth retardation and, in the limited data on food consumption, reduced food intake in parental male rats (F_{1b} and F_{2b} generations). Reproductive effects were only noted at 800 $mg.kg\text{-}diet^{-1}$. In light of the maternal toxicity, indicated by hypersensitivity and reduced body weight, the reproductive effects could be a corollary of such maternal toxicity. However, covariance analysis has indicated that the effects observed cannot be completely explained in terms of maternal body weight.

The NOEL for the present study is 100 $mg.kg\text{-}diet^{-1}$, the most sensitive parameters measured being male body weight gain reduction which may be a reflection of reduced food intake. Pair feeding studies would be required to confirm this possibility.

A three generation study on single comb white longhorn hens (Robinson 1968) is discussed in Section 4.3.1. This study indicated dietary levels of 200 $mg.kg^{-1}$ to be a NOEL for the parameters measured; general condition, mortality, body weight, food-consumption, efficiency of food utilization, egg-production, time to reach maturity, egg whites, fertility, hatchability, embryonic abnormalities and gross pathology. Growth retardation, delayed sexual maturity and reduced egg production were observed at 800 $mg.kg^{-1}$.

5.3.2 TERATOLOGY STUDIES

Teratology has been defined as "the study of the effects of intrinsic or extrinsic factors related to permanent structural or functional deviations arising during embryogenesis. A teratogenic agent is any agent which can induce or increase the incidence of congenital malformations" (HWC 1975).

There is a wide variation in the response of animal species to teratogenic agents and care must be exercised in ascertaining the

suitability of the test animal in predicting the potential response in humans. Although much of the early work in teratology was done in the developing hen egg, it is generally unacceptable as a system for predicting the teratogenic potential in man because of its ultra-sensitivity and lack of maternal-fetal relationships (HWC 1975).

A commonly accepted protocol for a teratology study involves dosing pregnant females during the period of embryogenesis, which in the rat is day 6 through 15, using at least three dose levels in addition to the appropriate control groups. The highest dose group should show signs of maternal and/or fetal toxicity to ensure that the dose level was sufficiently high. The usual method of administration is by oral intubation. The fetuses are then delivered by cesarean section on the day prior to term.

The teratogenic potential of aminocarb was assessed in the rat (Robinson et al. 1980). The test compound was given by oral intubation to four groups of 25 mated Sprague-Dawley rats on day 6 to 15 of gestation. Day 1 is considered to be the day of detection of evidence of mating. Three groups received 2, 6, and 18 mg.kg-BW^{-1} and a fourth group, a negative (vehicle) control, received only Poly-Ethylene Glycol 400 (PEG400). The dose was adjusted to changes in body weight, but the volume administered remained constant at 5 mL.kg^{-1}. Clinical observations were made daily by technicians and animals noted as abnormal were examined weekly by a veterinarian. Body weights were recorded on days 0, 6, 9, 12, 15 and 21. The fetuses were delivered by cesarean section on day 21 of gestation and the following fetal data were gathered: number of corpora lutea, number of fetuses and resorptions, fetal body weight, sex, and gross abnormalities. Approximately half of the animals were selected for skeletal examination (Alizarin-Red stained) and the remaining pups were fixed in Bouin's solution for examination of soft tissues.

Daily administration of the test compound at the highest dose level (18 mg.kg-BW^{-1}) resulted in tremors (in 11 of 25 rats) and chromodacryorrhea in the maternal rats. Diarrhea and soft feces were observed in all groups including the controls. The incidence was greatest in the 18 mg.kg-BW^{-1} group. A 20% maternal mortality (5/25), probably compound related, was observed in the high-dose group. No mortality was observed at 2 or 6 mg.kg-BW^{-1}. One control animal died, probably due to faulty intubations. Maternal body weight gain was reduced in all test groups, during the period of insult. Upon withdrawal of the test material, body weight gain recovered to control levels at 2 and 6 mg.kg-BW^{-1}, but not at 18 mg.kg-BW^{-1}. The non-gravid maternal weight (i.e. after removal of uterine content) was statistically significantly depressed at 6, 8, and 18 mg.kg-BW^{-1}.

Incidence of pregnant females surviving to day 21 was 72, 88, 72 and 60% at 0, 2, 6 and 18 mg.kg-BW^{-1}. The low incidence at 18 mg.kg-BW^{-1} was due to maternal mortality, since all 5 animals which died were pregnant. No effects of the test material were noted on resorption rate, litter size, pup weight or litter weight. The data do not

differentiate between live and stillbirths, which is a deficiency in the study. However the average litter size (presumably dead plus live young) appears to have been greater in the treated groups than in the control group.

The high-dose group in the teratogenicity study had a sex ratio of 0.7 female to male which may indicate a fetotoxic effect on female offspring, but this cannot be confirmed in the absence of historical results for controls; moreover, the mid- and low-dose groups had sex ratios of 1.2 and 1.1 respectively, with an excess of females. The sex ratio in the control group was 0.9.

In the teratogenicity study a variety of minor skeletal and visceral abnormalities occurred in approximately 1-8% of young from all groups. The only major malformation noted was a case of scoliosis of the spine from the upper thoracic to the lower caudal region in 1/94 fetuses examined for skeletal malformations in the 18 mg.kg-BW^{-1} group. At 6 mg.kg-BW^{-1}, a case of mild scoliosis was noted in 1/110 fetuses subject to skeletal examination. In addition, treated groups showed a higher incidence of reduction in the number of caudal vertebrae, which was non dose-related, enlarged anterior fontanelles in 5 mid-dose and 2 high-dose fetuses and a scattered incidence of other minor malformations.

Overall, these data are not indicative of teratogenic activity, although historical data on background incidence of scoliosis would be useful to confirm this conclusion.

Examinations for gross and microscopic soft-tissue abnormalities were carried out, though not listed separately. Mild hydrocephalus, abnormal position of the testes, or agenesis of one testis were reported only in 1 or 2 treated pups each.

The difference between the methods of administration of the test material mitigate any direct comparison between the multiple generation reproduction and the teratogenicity study but neither study shows aminocarb to have any significant discernible teratogenic effects in the rat at the doses tested (up to 10 mg.kg-BW^{-1}).

An additional teratology study is in progress utilising a second species (Howard 1982).

5.9.3 MUTAGENICITY STUDIES

In recent years there has been a thrust towards developing tests less lengthy and less difficult to interpret than the chronic animal tests.

Numerous *in vitro* screening tests have been developed, the best known of which is the Ames test. This test employs microbial cells which are exposed to the chemicals under different conditions and then

screened for mutations. It has been shown that in many instances, products capable of inducing mutations in an Ames test are also capable of inducing tumors in test animals. This large body of background data in animals has served to partially validate the Ames test as a predictor for the carcinogenic potential of a chemical. It must be kept in mind that the in vitro tests for mutagenicity or carcinogenicity were designed as screening tests and that the final answer to the question of carcinogenic potential should be obtained by testing the compound in question in well-conducted whole animal studies.

There are numerous other tests which allow identification of the site of genetic activity.

In addition to screening tests that may be useful in predicting the carcinogenic activity of a product, certain of the in vitro studies can be used to identify the potential of a compound to induce mutation per se. However, the same difficulties exist in extrapolating from microbes to man and from in vitro to in vivo responses. Therefore, considerable care must be taken in the interpretation of screening tests and "the potential for mutagenic effects in man should be estimated only after the results of testing in various experimental systems have been considered" (HWC 1975).

Aminocarb was found to be negative in an Ames test (Douglas 1982) but the concentrations are not known and hence a positive response at some concentrations cannot be ruled out. More extensive mutagenicity studies are in progress.

5.10 PERIPHERAL TOXICOLOGICAL ISSUES

5.10.1 REYE'S SYNDROME AND VIRAL ENHANCEMENT

Over the past few years attention has focused on the possible link between the aerial application of pesticides for the control of spruce budworm and the incidence of Reye's syndrome.

Reye's syndrome was first reported in detail in Australia in 1963 (Reye et al. 1963). It occurs most commonly in children from infancy to early teens. The disease is a biphasic process beginning with a mild illness characteristic of an upper respiratory infection or chicken pox, and lasting three to seven days. After these initial symptoms, a period of relative recovery occurs which leads into rapid clinical deterioration. Fever, vomiting, profound alteration in brain function and fatty degeneration of the liver, kidney, heart and pancreas occur in a period of one to six weeks. Presentation is somewhat different in infants with less vomiting and more respiratory involvement in the prodromal phase (Huttenlocher and Trauner 1978).

It is generally accepted that a liver biopsy must be done to prevent misdiagnosis of Reye's syndrome since the liver changes are specific (Bove et al. 1975; Partin 1975). Elevations in serum trans-

aminase levels and blood ammonia levels are observed in the majority of patients. Changes in blood glucose levels do not appear to be as diagnostic, with hypoglycemia appearing more frequently in infants (Huttenlocher and Trauner 1978). A very consistent finding in Reye's syndrome is a normal or only slightly elevated serum bilirubin level, despite the marked abnormalities in other liver function tests. This discrepancy helps to set apart cases of Reye's syndrome from other forms of liver disease (Huttenlocher et al. 1969). The spinal fluid examination is unrevealing in these cases. The spinal fluid pressure may be elevated, but cell and protein values are normal. The spinal fluid sugar is usually low and tends to parallel the low serum values when these determinations are done simultaneously. Numerous other parameters have been reported to be altered in Reye's syndrome, but no consistent pattern is readily apparent (Kang 1979; Ch'ien et al. 1979; Trauner et al. 1977; Rittenhouse et al. 1979; Applegarth et al. 1979; Faraj et al. 1979; Chaves-Carballo et al. 1979; Shaywitz et al. 1979).

The central nervous system disturbances, due to cerebral edema, are classified into five clinical stages ranging from lethargy, disorientation, coma, decerebrate rigidity, to respiratory arrest and death (Kang 1979). The prognosis is poorer for patients who have stage IV or stage V coma, and the neurological sequelae appear to be related to the severity of the coma (Corey et al. 1977).

The relationship between the brain damage, fatty liver and biochemical changes cannot be fully explained, thus making treatment purely empirical (Huttenlocher et al. 1969). Exchange transfusions (DeVivo et al. 1975; Berman et al. 1975), brain decompression, blood and glucose infusion and general supportive care are the current modes of treatment. A summary of treatment is discussed in a recent paper by Crocker and Bagnell (1981). The mortality rate has declined dramatically in the past few years to 10 to 20%, due to more rapid diagnosis and immediate treatment (DeVivo 1978).

The exact cause of Reye's syndrome is unknown. It is generally accepted that it is multifactorial, and viruses, genetic predisposition, endogenous and exogenous factors have been implicated.

Epidemiology has been utilized in an attempt to understand the etiology of Reye's syndrome. An epidemic of Reye's syndrome in the United States in 1974 prompted intensive surveillance and study of nationwide occurrence (Corey et al. 1976). In this outbreak of Reye's syndrome, the four identified potential prodromal viruses were:

(1) Upper Respiratory Illness (U.R.I.)
(2) Influenza B
(3) Varicella (chicken pox)
(4) Gastrointestinal Infection.

The data indicated that in Reye's syndrome patients over 10 years of age, U.R.I. and Influenza B were the most frequent prodromes, and that the median age of the patients was 11 years. The conclusion was that

Reye's syndrome was affiliated with U.R.I. and influenza B. Influenza B outbreaks commonly occur between January and March, and the Reye's syndrome cases closely parallel this. Other studies have indicated that Reye's syndrome is associated with influenza A (e.g. Reuben 1979), particularly the H1N1 strain (CDC 1982).

The data on geographic distribution in the U.S. are conflicting. One study showed a greater incidence of Reye's syndrome in rural areas over urban areas (1.8 cases/100,000 population versus 0.5/100,000) (Hattwick and Sayetta 1979). This difference cannot be explained by occurrence of influenza B, since it was the same in both areas (DeVivo et al. 1975). A study (Nelson et al. 1979) which included a 16-month national surveillance period and a five-year population-based retrospective study in Ohio showed a lower incidence in rural areas with the highest incidence actually being in suburban areas. The attack rate for blacks was not statistically different from whites contrary to the higher incidence in whites discussed in Hattwick's study (Hattwick and Sayetta 1979). It would be premature to state whether Reye's syndrome is an urban, suburban or rural disease and to attempt to isolate potential environmental factors which may be unique to one of these areas. These two studies suggest that a viral prodrome is epidemiologically associated with Reye's syndrome, with influenza B being the most common during the winter months. Association with antecedent illnesses other than influenza B occurs in early fall to late spring (Nelson et al. 1979).

The incidence of Reye's syndrome in Canada is not known. However, estimates of incidence in the Maritime provinces (Bagnell et al. 1978) suggest that it is similar to that of the U.S.: 0.75 cases per 100,000 population in New Brunswick versus 0.4-1.8 cases per 100,000 population in the U.S. (Hattwick and Sayetta 1979). The incidence of 0.09 cases per 100,000 population in Nova Scotia appears to be unusually low.

It is evident that Reye's syndrome is closely associated with specific viral illnesses. The question as to why some children proceed from the viral prodrome to the subsequent stages of Reye's syndrome is difficult to answer. Some children may be more susceptible to viruses due to inborn errors of metabolism such as enzyme deficiencies in the urea cycle (Thaler et al. 1974), or abnormal immunological responses (Linnemann 1974). The increased incidence in siblings (Hilty et al. 1979) and twins (Thaler et al. 1970) lends support to the concept of genetic predisposition.

It is not yet possible to ascertain whether these genetic anomalies are in fact analogous to Reye's syndrome or whether they lead to symptoms which are similar. The marked changes in the mitochondria and subsequent metabolic effects are common to the reported cases of enzyme defects and to Reye's syndrome, but there are insufficient data at this time to establish whether these are primary or secondary effects.

There have been reports suggesting that endogenous factors which affect the mitochondria, both morphologically and functionally, might be the causative agents. The endogenous factor that Aprille and co-workers reported to have an effect on mitochondria (Aprille and Asimakis 1979) has subsequently been identified as being uric acid (Aprille et al. 1980). This would not appear to be the primary endogenous factor but may result from metabolic changes caused by some as yet undiscovered factor. The exogenous factors which have been implicated in the etiology of the syndrome include aflatoxins (Ryan et al. 1979), pentenoic acid (Mullen 1978), salicylates (Christofferson et al. 1980; CDC 1982) and emulsifiers (Crocker et al. 1976). The hypothesis is that the chemical could in some way alter susceptibility to the virus. There is evidence that in insects, a combination of pesticide and virus enhances mortality (Pollack 1979). The mechanism is not understood and could be either a chemical synergist of the virus, where viral production could be stimulated or susceptibility to infection could be increased, or viral synergist of the chemical where the virus might prevent detoxification of the chemical.

Various animal models have been developed in which the interaction of chemicals and viruses have been tested. Ducks pretreated with PCBs and then exposed to duck hepatitis virus (Friend and Trainer 1970) and mice pretreated with the emulsifier Toximol MP8 (a mixture of anionic and nonionic surfactants, no longer used in Canadian spray programs) and then exposed to EMC virus (Crocker et al. 1976) or influenza B virus (Crocker et al. 1981), both showed a combination or synergistic effect. Lymphocytes from Toximol MP8 treated mice responded poorly to interferon induction relative to lymphocytes from control mice (Rozee et al. 1982). Reuben (1979) did not observe any synergistic or viral chemical interaction in hamsters pretreated with a variety of chemicals, including pesticide active ingredients, solvents or emulsifiers, and then exposed to influenza A or B.

Clearly, a viral-chemical interaction can occur in certain species under certain conditions. However, the differences between the response in the test animals and Reye's syndrome in humans complicate any comparison with the disease entity in humans (Crocker and Bagnell 1981) and raise doubts as to the validity of these animal models for predicting the mechanism of Reye's syndrome in humans (Tower 1979).

In addition to these in vivo models, in vitro experiments have involved incubating cells with the chemical before exposure to the virus. In one system (Rozee et al. 1979) mouse L929 fibroblasts were subsequently infected with vesicular stomatitis virus (VSV) or encephalomyocarditis virus (EMC). When this system was used to examine the replicative cycle of EMC virus (Lee et al. 1980) the authors reported that the emulsifier Toximul MP8 appeared to increase the rate of virus penetration and uncoating, although similar amounts of virus were absorbed by treated and control cells. They also reported that the cell's response to interferon inducers was adversely affected and an

already established interferon antiviral state was reversed. The authors proposed that one or more of these actions resulted in the observed statistically significant enhancement of the cell's susceptibility to virus.

The extrapolation of data from any in vitro testing system to humans is difficult. L929 fibroblasts are a serially propagated line characterized by rapid proliferation, unlike human liver cells which divide only very slowly. Also, neither VSV or EMC virus have been implicated in Reye's syndrome; Lee et al. (1980) note that whether the mechanisms they report "are operative in the pathogenesis of Reye's syndrome is not answered by these experiments".

Peripheral blood lymphocytes obtained from Reye's syndrome patients in the acute phase of the disease have been reported to produce significantly less interferon, after induction with Newcastle disease virus, than lymphocytes from recovery patients or controls (Rozee et al. 1981, 1982). The authors interpret this result to implicate interferon in the altered viral response of Reye's syndrome.

An infectivity enhancing ratio of 2 has been arbitrarily assigned to be of biological significance (Rozee et al. 1978). Aminocarb was reported (Rozee et al. 1978) to have a ratio of 2.5 and 2.1 in in vitro experiments. The insecticide diluent 585 was not found to be an enhancer.

New tests including viral enhancement are being continually evaluated for their usefulness as predictors of toxicity to humans. These tests can be useful in screening for potentially hazardous chemicals, but the results from in vitro tests must be carefully weighed in light of whole animal data to ensure relevance. This is of paramount importance in the study of toxic substances because many, if not all, of the processes and interactions which can occur in the animal are absent in an in vitro system. In conclusion, the relevance of results generated from the viral enhancement model in predicting human health hazards remains to be established.

5.10.2 NITROSATION OF CARBAMATES

Questions were raised in the past as to whether aminocarb might be converted into a nitroso derivative. These concerns apparently stemmed from indications that carbaryl, which is also a carbamate insecticide, can be converted into nitrosocarbaryl which is a mutagen (Elespuru et al. 1974; Regan et al. 1976; Blevins et al. 1977a,b; Egert and Greim 1976; Quarles and Tennant 1975) and a carcinogen (Lijinsky and Taylor 1976). In a skin painting study, results were however negative (Lijinsky and Elespuru 1975).

The critical issue in the case of aminocarb, or any other carbamate, is to determine whether nitrosation is even chemically

feasible, and whether it can occur in toxicologically significant levels, either from conversion in the environment, or in the gut.

Relatively large amounts of secondary amines or their precursors (50-500 $mg.kg^{-1}$ N), and of nitrite or nitrate (10-100 $mg.kg^{-1}$ N) are required for the formation of measurable amounts ($mg.kg^{-1}$ range) of nitrosamines in soil. Studies in which high concentrations of amine herbicides were added to soil resulted in no detectable residues of nitrosamine (Tate and Alexander 1976). A detailed search of the literature (up to 1978) revealed no publications on the production of nitrosamines from aminocarb either in the laboratory or in nature.

Although it may be possible to produce a nitrosated product in the test tube under carefully controlled conditions, the situation may be completely different in a biological system. The possibility that carbaryl, a carbamate pesticide, might react with nitrite in the stomach to produce nitrosocarbaryl has been tested. In one study the mutagenic potential was investigated in a micronucleus test in Swiss mice. Carbaryl and sodium nitrite were administered together, and the bone marrow smears which were evaluated showed no aberration of micronuclei incidence (Seiler 1977). A second study determined whether sufficiently high levels of nitrosocarbaryl were produced in the gut of pregnant rats to induce tumors in the offspring and incidentally in the mother (Lijinsky and Taylor 1977). Tumor incidence was unaffected. In a more recent study, actual levels of nitrosocarbaryl produced in the gut in rats (pH 3.5) and guinea pigs (pH 1.5) under various test conditions were measured (Rickard 1979). Simultaneous intubation of solutions of 1 µmol of carbaryl and 1160 µmol of sodium nitrate resulted in a 0.02% yield in the rat and approximately 1% in the guinea pig. The nitrosation was dependent on the nitrite dose but not on the carbaryl dose (0.025-2.5 µmol). At the lowest nitrite dose of 7 µmol, a 0.01% yield of nitroso-carbaryl was obtained and at a dose of 1160 µmol, a 1.5% yield was determined. When the reactants administered were mixed with the feed in guinea pigs, nitrosation yields were "not substantially different".

The pH of the stomach contents in man ranges from 2 to 3 (Guyton 1971) and Rickard's data indicate that the yields of nitrosamine drop dramatically from 15% at pH 2 to trace amounts (0.01%) at pH 3.

These data support the findings of Lijinski that the small amounts of nitrosamine formed were insufficient to induce cancer in developing fetuses, and also support the long-term studies in which no carcinogenicity was detected when carbaryl was administered in the feed for the lifetime of the animal. The oral exposure to aminocarb from forestry applications would be extremely low, and thus the risk of developing cancer would be low, even if nitrosamines are formed. The negative results seen in the study in which nitrosocarbaryl was painted on the skin (Lijinsky and Elespuru 1975) would suggest negligible risk through dermal exposure, which is the route whereby most of the exposure would occur in a forestry operation.

Appendix I. Use of formulated[α] aminocarb in eastern North America 1970 to 1980. Rates in AI.

	Ontario	Quebec	New Brunswick	Newfoundland	Maine
1980	4,800 ha 1 x 87 g.ha^{-1}[β] 2 x 87 g.ha^{-1}[β]	28,000 ha 2 x 52 g.ha^{-1}[β] 1 x 87 g.ha^{-1}[β]	247,000 ha 2 x 70 g.ha^{-1}[β]	-	-
1979	15,000 ha 1 x 63 g.ha^{-1}[γ] 1 x 87 g.ha^{-1}[β]	556,000 ha 2 x 52 g.ha^{-1}[ζ] 1 x 52 g.ha^{-1}[ζ] 2 x 52 g.ha^{-1}[ζ] + fenitrothion 1 x 52 g.ha^{-1}[ζ] + fenitrothion	1,560,000 ha 2 x 70 g.ha^{-1}[β] 1 x 87 g.ha^{-1}[β]	-	-
1978	160 ha 2 x 87 g.ha^{-1}[ε] 1 x 87 g.ha^{-1}[ε] + acephate	1,010,000 ha 2 x 52 g.ha^{-1}[ζ] 1 x 70 g.ha^{-1}[β] 2 x 52 g.ha^{-1}[ζ] + fenitrothion 1 x 52 g.ha^{-1}[ζ] + fenitrothion 1 x 70 g.ha^{-1}[ζ] + fenitrothion	737,000 ha 2 x 70 g.ha^{-1}[β] 1 x 70 g.ha^{-1}[β]	376,000 ha 2 x 70 g.ha^{-1}[β]	1,200 ha 1 x 168 g.ha^{-1}[η]
1977	3,800 ha 2 x 70 g.ha^{-1}[β] 1 x 70 g.ha^{-1}[β]	35,000 ha 1 x 70 g.ha^{-1}[ζ]	517,000 ha 2 x 52 g.ha^{-1}[ζ] 2 x 70 g.ha^{-1}[β] 2 x 70 g.ha^{-1}[β] + fenitrothion	486,000 ha 3 x 70 g.ha^{-1}[β] 2 x 87 g.ha^{-1}[β] 1 x 87 g.ha^{-1}[β] + fenitrothion	120 ha 1 x 168 g.ha^{-1}[η]
1976	21,900 ha 2 x 105 g.ha^{-1}[δ] 1 x 105 g.ha^{-1}[δ] 1 x 105 g.ha^{-1}[δ] + fenitrothion	23,000 ha 2 x 52 g.ha^{-1}[ζ] 1 x 52 g.ha^{-1}[ζ]	315,000 ha 2 x 70 g.ha^{-1}[β] 2 x 52 g.ha^{-1}[δ] 2 x 70 g.ha^{-1} + fenitrothion or phosphamidon 1 x 70 g.ha^{-1} + fenitrothion or phosphamidon	-	60 ha 1 x 168 g.ha^{-1}[η]
1975	-	524,600 ha 2 x 52 g.ha^{-1}[δ] 1 x 52 g.ha^{-1}[δ] + fenitrothion	64,000 ha 2 x 52 g.ha^{-1}[ζ] 1 x 52 g.ha^{-1}[ζ]	-	1,200 ha 1 x 168 g.ha^{-1}[η]
1974	-	485,000 ha 2 x 52 g.ha^{-1}[ζ]	-	-	-
1973	-	132,000 ha 1 x 52 g.ha^{-1}[ζ]	-	-	-
1972	-	31,100 ha 1 x 52 g.ha^{-1}[ζ]	-	-	-
1971	-	-	19,400 ha 1 x 105 g.ha^{-1}[β] 1 x 35 g.ha^{-1}[β]	-	-
1970	-	-	2,000 ha 1 x 87 g.ha^{-1}[β]		

[α] Prior to 1978, No. 2 fuel oil, diesel oil or Aerotex was the commonly used diluent with Matacil. In 1971, 9700 ha in New Brunswick were sprayed with a wettable powder in summer oil. Since 1978, diluent 585 has been used in all Canadian programs.

[β] Applied in 1.4 L.

[γ] Applied in 1 L.

[δ] Applied in 0.8 L.

[ε] Applied in 4.7 L.

[ζ] Applied in 1.1 L.

[η] Applied in 2.2 L.

References

Canadian Forestry Service (1981), Carrow et al. (1980), Carter (1979), Nigam (1980), Webb (1980).

APPENDIX II. SUMMARY OF PHYSICAL, CHEMICAL AND SPECTRAL PROPERTIES OF AMINOCARB AND ADJUVANTS

II.1 p-DIMETHYLAMINO-m-TOLYL N-METHYLCARBAMATE (ACTIVE INGREDIENT)

II.1.1 PHYSICAL AND CHEMICAL PROPERTIES

Appearance	Beige crystalline solid
Molecular weight	208.3
Melting point	93 - 94°C
Boiling point	Not available
Vapor pressure	1.7×10^{-5} mm Hg[α] at 20°C, 2.0×10^{-5} mm Hg at 25°C, 3.3×10^{-5} mm Hg at 30°C, 6.8×10^{-5} mm Hg at 35°C, 9.3×10^{-5} mm Hg at 40°C, (Addison 1981b)
Solubility	see Section 2.1.1
Octanol-water partition-coefficient	see Table II.1
pKa	aminocarb - 5.65; aminocarb phenol - 5.95, 10.05 (Weinberger and Greenhalgh 1981)

II.1.2 SPECTRAL PROPERTIES

UV (C_2H_5OH)	λ_{max} = 248.5 nm
	$\varepsilon_{max} = 6.67 \times 10^4$ L.m^{-1}.cm^{-1}
	$\varepsilon_{300} = 7.32 \times 10^3$ L.m^{-1}.cm^{-1}
IR ($CHCl_3$)	3460 cm^{-1} (N-H) 1738 cm^{-1} (C=O)
NMR (60 MH_E)	δ = 2.38 (s. 3H, aryl-CH_3) 2.72 (s. 6H, aryl NCH_3) 2.95 (d. 3H, CO-$NHCH_3$) 6.08-6.92 (3H, unresolved aryl protons)

[α] 1 mm Hg = 0.133 kPa at 0°C.

MS (EI)	151 (base peak), 150, 135, 208 (parent), 152, 120, 134, 121, 51, 77 m/E
	The mass spectrums A, MA, MAC, MAA, AA, AC, FA, FC, MFA and MFC[β] are presented in Figures II-1 through II-10
TLC	See Table II-2

β See inside back cover for key to names

Table II-1. Octanol:water partition coefficient of aminocarb (Weinberger and Greenhalgh 1981).

K_{ow}	pH
1.8 ± 0.3	4.0
8.2 ± 1.8	5.0
30 ± 10	6.0
58 ± 6	7.0
70 ± 10	8.0
80 ± 10	9.0

Table II-2. R_f values of aminocarb and derivatives on silica gel (Flint 1981).

Compound	Solvent System[α] A	B	C
Aminocarb (A)	0.72	0.75	0.76
Methylamino formylamino aminocarb (MFA)	0.29	0.24	0.50
Formylamino aminocarb (FA)	0.24	0.22	0.18
Amino aminocarb (AA)	0.39	0.41	0.41
Methylamino aminocarb (MAA)	0.60	0.64	0.62
Aminocarb phenol (C)	0.74	0.81	0.39
Formylamino aminocarb phenol (FC)	0.25	0.32	0.10
Amino aminocarb phenol (AC)	0.41	0.66	0.29

[α] A acetonitrile:benzene:hexane (1:1:1)

B isopropyl ether:acetonitrile (4:1)

C chloroform:ethanol (95:5)

II.2 SPECIFICATIONS FOR DILUENT 585 (AGRICULTURE CANADA 1978)

Virgin Distillate	100%
Distillation end point	max. 307.2°C (585°F)
Pour point	max. -23.3°C
Flash point	min. 51.7°C
Kinematic viscosity	1.4-3.0 Centistokes (37.8°C)
Corrosion	max. No. 1 (3 h at 100°C)
Sulphur	max. 0.25% by weight
Mercapta sulphur	max. 10 mg kg^{-1}
Strong acid number	0
Strong base number	0
Saybolt color	min. + 18
Aniline color	max. 62.7°C
Density	0.825 $g.mL^{-1}$ (at 15°C)

II.3 NONYL PHENOL

Appearance	Pale yellow, highly viscous, liquid with slight characteristic phenolic odor.
Molecular weight	215
Vapor pressure	2 mm Hg[α] at 130°C, 3.5 mm Hg at 140°C, 20 mm Hg at 180°C
Solubility	Soluble in benzene, chlorinated solvents, aniline, heptane, aliphatic alcohols and ethylene glycol. Insoluble in water
Distillation range	291-300°C

[α] 1 mm Hg = 0.133 kPa at 0°C.

Hydroxyl number	253
Specific gravity	0.950
Refractive index (N_D^{20})	1.513
Dielectric constant (3500 kc, 23°C)	5.0
Flash point (TOC)	148.8°C
Color (Pt-Co scale)	75

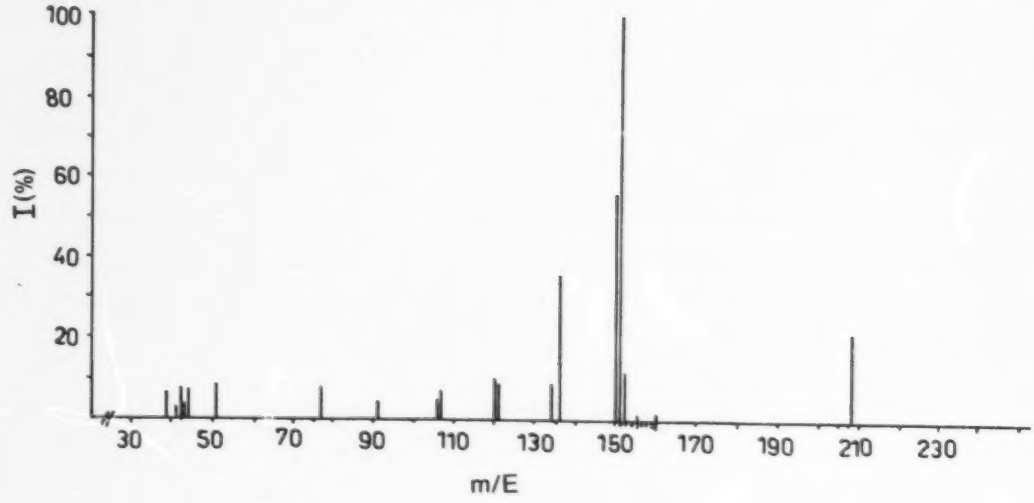


Figure II-1. Mass spectrum of A.

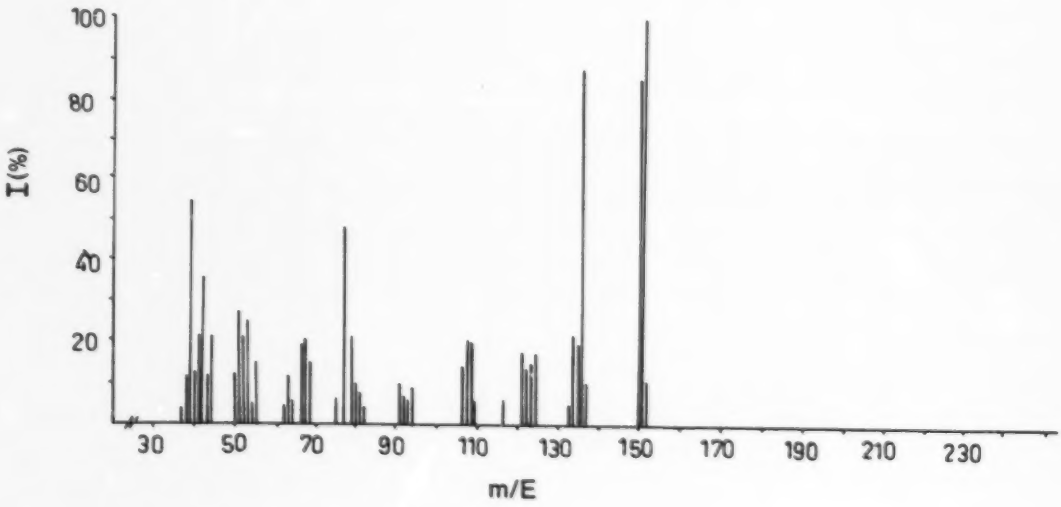


Figure II-2. Mass spectrum of MA.

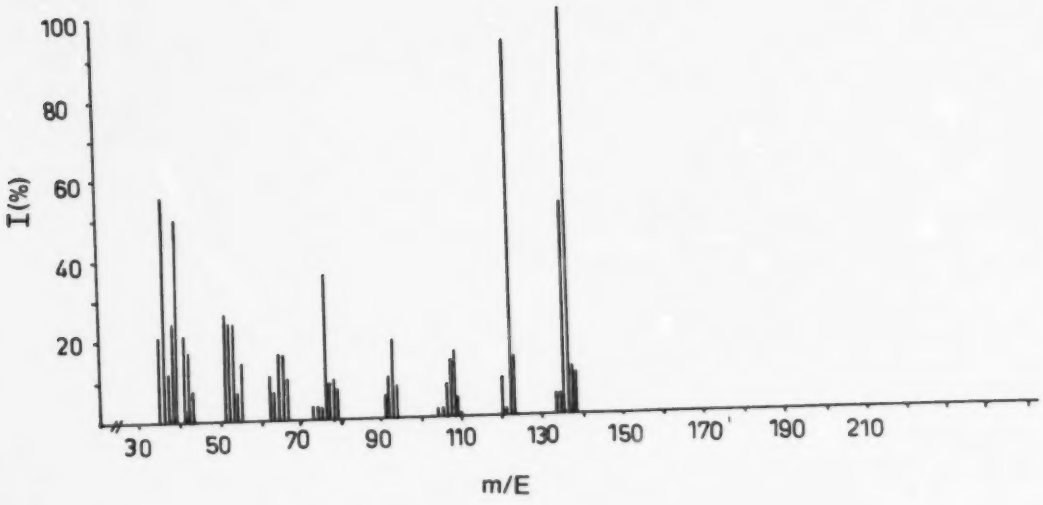


Figure II-3. Mass spectrum of MAC.

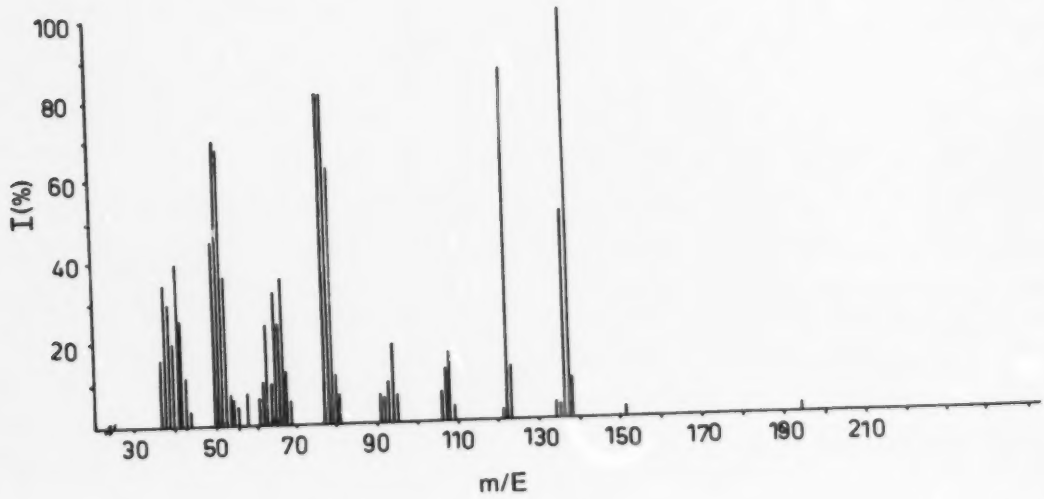


Figure II-4. Mass spectrum of MAA.

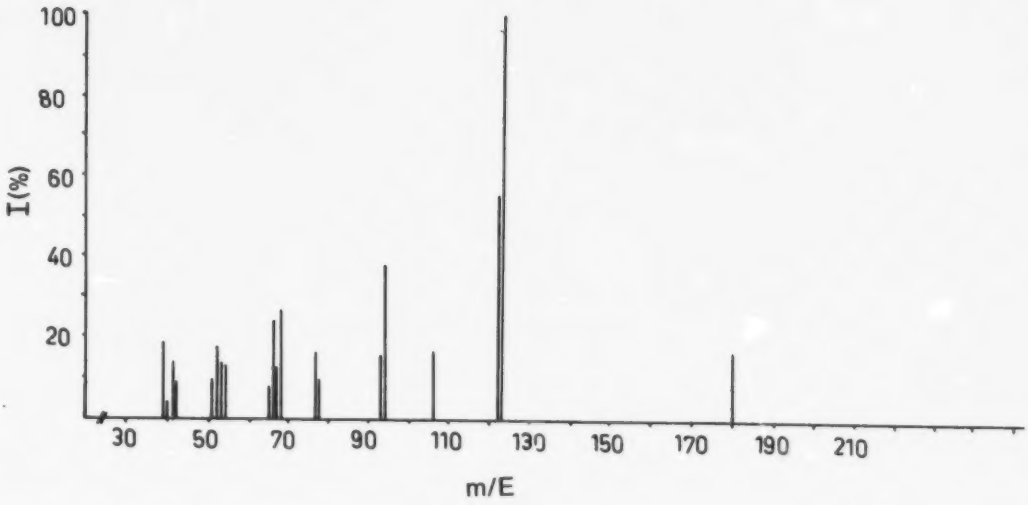


Figure II-5. Mass spectrum of AA.

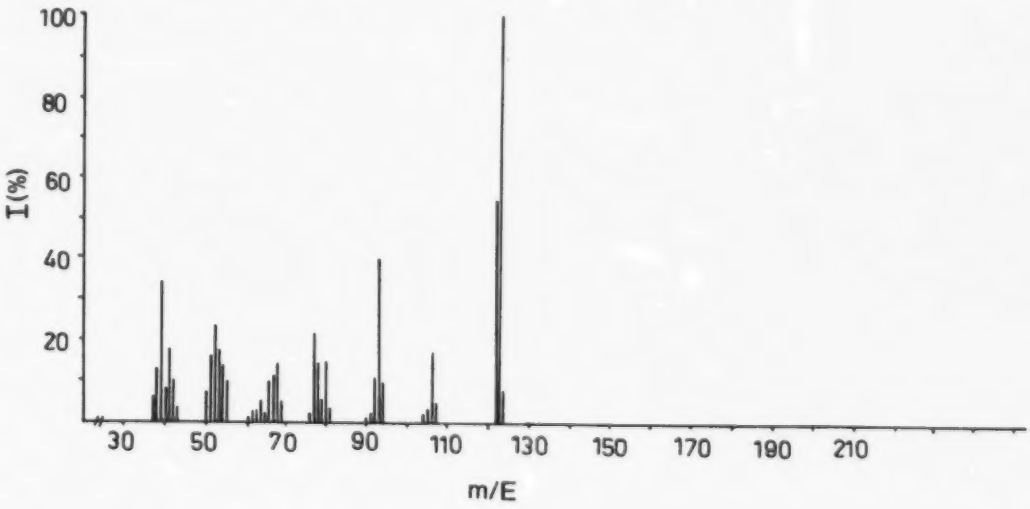


Figure II-6. Mass spectrum of AC.

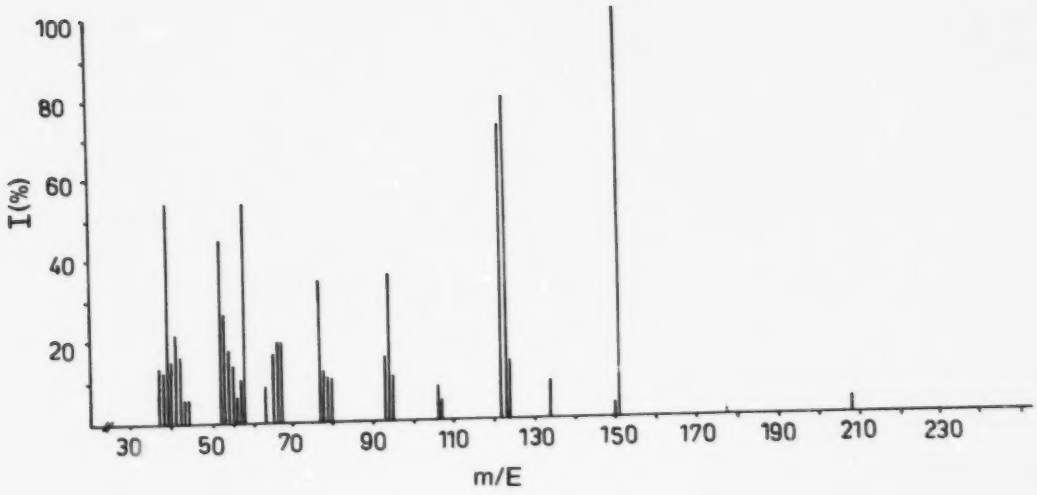


Figure II-7. Mass spectrum of FA.

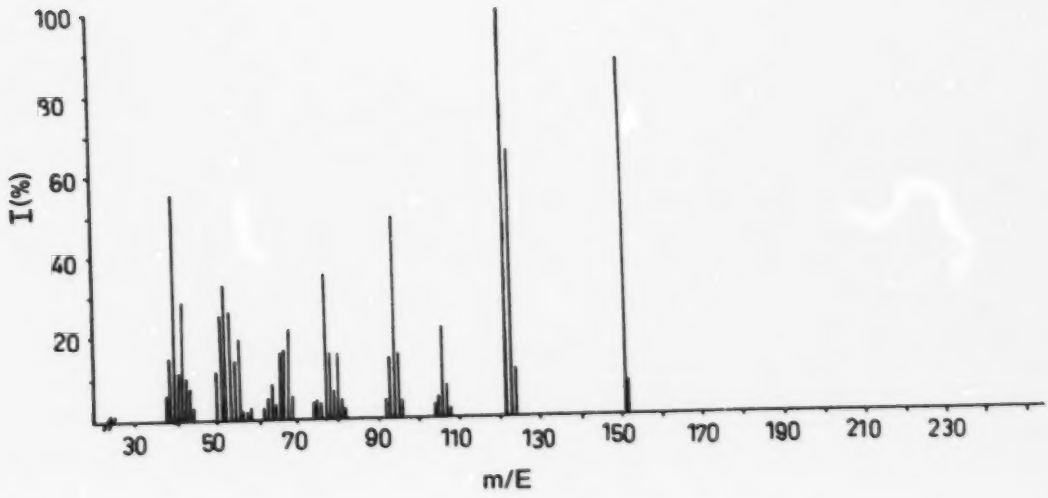


Figure II-8. Mass spectrum of FC.

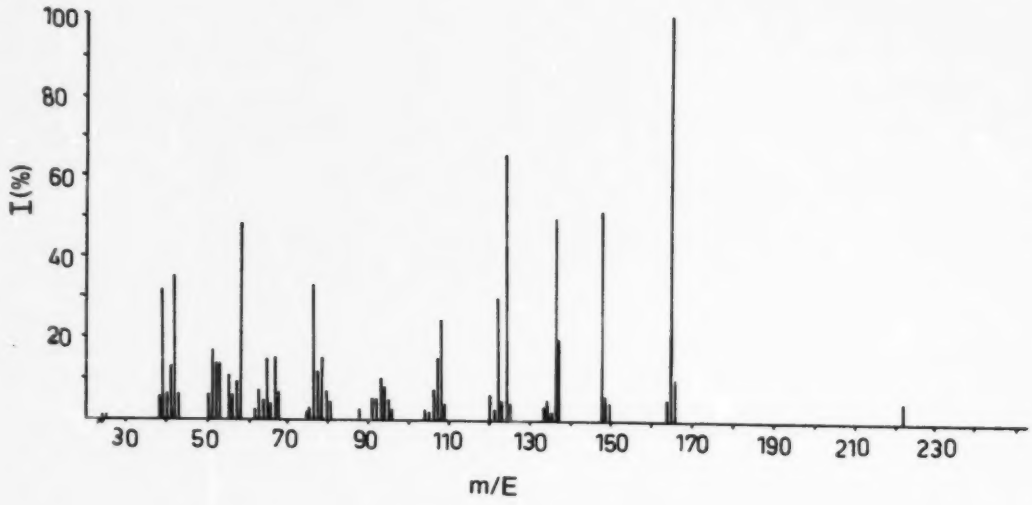


Figure II-9. Mass spectrum of MFA.

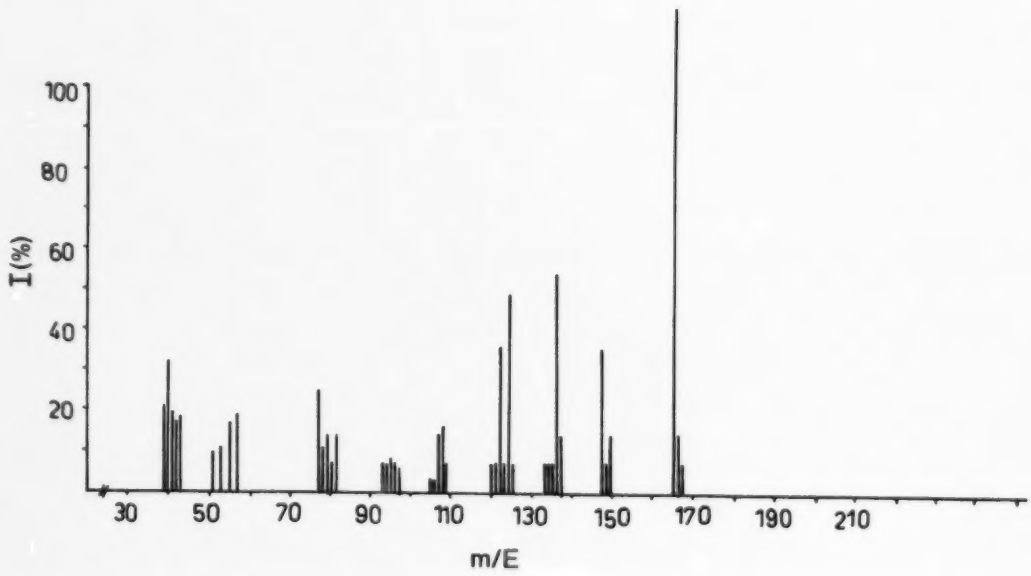


Figure II-10. Mass spectrum of MFC.

APPENDIX III MODEL COMPUTATIONS OF DRIFT, DEPOSITION AND EXPOSURE

III.1 MODEL INPUT

III.1.1 THE SPRAY SCENARIO

The following spray scenario is adopted in the present model:

1) A uniform spruce fir forest of mean height 16 m.

2) A 3-aircraft team of TBMs[α] spraying at an airspeed of 150 kts (77 $m.s^{-1}$) and equipped with TEEJET 11010 nozzles to atomize oil-diluted Matacil OSC.

3) Neutrally stratified meteorological conditions with an ambient temperature of 5°C at spray height and a mean wind speed profile giving 0.25 $m.s^{-1}$ at mid-upper canopy height, increasing exponentially to 0.5 $m.s^{-1}$ at tree height, and then logarithmically to 2.5 $m.s^{-1}$ at 50 m above the trees.

Spruce-fir stands, which reach a height of about 14-18 m when mature, are typical of New Brunswick forests. The weather situation in this scenario approximates that shortly after dawn, in early spring, at N.B.-Quebec latitudes, on those occasions when aerial spraying is conducted against the spruce budworm. Stronger winds would reduce the time-integrated concentration at the spray line, although dermal impaction would be increased. The light wind speed regime has been adopted for the computations described here, since it approximates usual field spraying conditions. Since the vortex wake which contains the spray is a fluid material volume, the insecticide is constrained to reach the forest at least as quickly as the vortices, a fact which minimizes the relevance of the spraying altitude. For computational purposes, a value of 37 m is adopted for the aircraft spray height above ground level (agl).

The components of the Matacil OSC spray follow current New Brunswick practice and are given on a per hectare basis below:

Component	Amount
Aminocarb	0.070 kg
Nonyl Phenol	0.18 kg (0.19 L)
585 Oil	1.25 L

The resultant volume per hectare is 1.50 L.

Following atomization of the spray the droplets are assumed to evaporate at the rate given in Picot et al. (1980) for pure 585 oil

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[α] Grumman WW-II torpedo bombers modified for aerial spraying.

droplets, inasmuch as this diluent constitutes about 83% of the droplet volume and the vapor pressure of the oil is much larger than that of the aminocarb and nonyl phenol component. The initial drop-size distribution differs from that for pure 585 oil because of the addition of the aminocarb and nonyl phenol. The calculated modification of the basic oil droplet spectrum of Tomney et al. (1978) is based on the method of Ingebo and Foster (1957), using values of spray viscosity and surface tension appropriate to the New Brunswick spray formulation[α]. This gave a maximum droplet diameter of between 200 and 250 μm and a volume median diameter of about 100 μm, vs. ~ 160 μm and ~ 80 μm respectively for the basic spectrum. Knowledge of the droplet spectrum and evaporation is important because the model-predicted aerosol concentrations for individual droplet sizes must be weighted by the droplet mass distribution to generate the overall concentration field.

III.1.2 SOURCE CONFIGURATION

Matacil is sprayed in crosswind swaths spaced at intervals of 410 m since this figure is judged by New Brunswick spray operators to be the overall swath width of a 3-aircraft team of TBMs. An application of 1.50 $L.ha^{-1}$ then corresponds to 0.062 L per metre of flight line, or to a model line source strength of 2.87 $g.m^{-1}$ of aminocarb distributed on average over a 410 m-wide swath. The vortex wake transports this material toward the upper canopy at a descent speed assumed to be 75 $cm.s^{-1}$ based on observations by Tennankore et al. (1980). The result would be an irregular aerosol cloud extending from about mid-canopy to somewhat above the trees after the vortices dissipate. However, for computational purposes the cloud configuration at this point is assumed to be rectangular with depth 6 m and the base located at 12 m agl, i.e. at mid-upper canopy height.

Other initial cloud configurations may be more realistic in terms of the initial depth of penetration of the cloud into the canopy. For example, ideal fluid theory suggests a final vortex height of about 40% of the spray plane wingspan which would place the cloud between 3 and 9 m agl. However, in their numerical study of droplet dispersion within the canopy, Picot and Kristmanson (1980) note that the initial cloud position must be higher than this to improve agreement between prediction and observation, although they do not recommend a particular height. Consequently the cloud is positioned between 12 and 18 m agl in the present model and the transfer of droplets into the lower canopy, as well as droplet collection by the foliage, is then computed following the methods of Wesley et al. (1977), Belot et al. (1976) and Picot and

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α The author is grateful to Dr. A. Sundaram of Forest Pest Management Institute for her measurements of spray viscosity and surface tension.

Kristmanson (1980). The space-time variation of the airborne droplet concentration field in the mid-upper canopy is also calculated. Sequential swaths are sprayed at intervals of 1-2 min, each 410 m further upwind than its neighbor, so that they will, on average, merely reproduce the concentrations predicted here, at the appropriate downwind distance.

III.2 RESULTS

III.2.1 INITIAL MASS DISTRIBUTION OF DROPLETS

The initial mass distribution of spray droplet referred to earlier is plotted in Figure 3-1 (Chapter 3). The ordinate is relative mass so that the area under the curve is unity. As time proceeds this spectrum shrinks due to 585 oil evaporation and the rapid loss of large droplets through sedimentary and turbulent deposition. The mean droplet diameter of the distribution of Figure 3-1 is 69 μm so that the atomization of 1.5 L of spray generates about 9×10^9 droplets.

III.2.2 TARGET-AREA DEPOSITION

Computations for the percentage of aminocarb mass deposited into the forest within the 410-m swath are given in Table III-1 as a function of initial droplet diameter (Do). The integrated result over the whole droplet-size spectrum is also shown. The deposition is divided into mid-upper canopy collection and the total transfer to lower levels. In this model 11.2% of the aminocarb is deposited into the mid-upper canopy within the swath. The result is sensitive to the foliage area density. For example doubling this from the model value of 4 $m^2.m^{-2}$ to 8 $m^2.m^{-2}$ increased the deposition of 100 μm diameter droplets in the upper level by 75%. Judging from the data of Belot et al. (1976) and Picot and Kristmanson (1980) it is not clear whether a value of 4 $m^2.m^{-2}$ is more realistic than 8 $m^2.m^{-2}$; measurements in the New Brunswick forest by Picot and Kristmanson (1980) suggest the value of 4 $m^2.m^{-2}$ which is adopted here.

During the initial vortex-controlled descent from spraying altitude, 21% of the spray mass evaporates to 585 oil vapor. Changing the aircraft spray height from the model value of 37 m agl would alter this figure.

III.2.3 AIRBORNE INSECTICIDE CONCENTRATION

The model-predicted concentration of aminocarb in air has a uniform maximum value everywhere within the initial 6 × 410-m swath. In reality, six locally high concentration regions would initially exist within this cloud due to three pairs of aircraft vortices so that isolated peaks approximately five times higher than the computed

Table III-1. Percentage of aminocarb mass deposited in 410-m swath as a function of initial droplet diameter.

Initial Droplet Diameter Do μm	W_s[α] $cm.s^{-1}$	Mid-upper canopy (%)	Below mid-upper canopy (%)
25	1.7	4.7	44.9
50	6.6	11.9	56.0
75	14.1	13.5	72.2
100	23.3	12.2	85.1
150	43.6	8.4	90
200	63.4	6.6	92
Cumulative		11.2	78.9

[α] Terminal velocity.

maximum (with lower values in between) could be expected, judging from the vortex descent model of Wickens (1980). However, a sample calculation for 100 μm diameter droplets showed that wind shear and turbulence smooth out such disturbances in about 2 minutes so that the assumption of an initially uniform distribution is not unreasonable. In particular, the dosage or time-integrated concentration at a point would change only nominally with this change of configuration. Note that all the nonyl phenol, as well as a varying amount of 585 oil depending on distance, resides in each airborne droplet along with the aminocarb.

The model-predicted, time-dependent, concentration profiles of the aminocarb component of the spray are shown in Figure 3-2 (Chapter 3). In this plot, time = 0 coincides with the arrival of the spray cloud at the canopy and x = 0 denotes the downwind edge of the cloud at this time. The time-dependent concentration profile within the 410-m swath is given by that at x = 0. Because of droplet collection by the foliage, the maximum atmospheric concentrations in the first 16 m agl occur at treetop. The absolute maximums are found a few metres above the trees, but are not plotted here, inasmuch as the goal of this calculation is the prediction of concentration of airborne aminocarb within the upper canopy.

III.2.4 THE DEPOSITION PATTERN

Figure III-1 shows the aminocarb deposition pattern as a function of distance from the upwind edge of the canopy swath (x = -410 m). The model predicts almost uniform deposit within the swath owing to the assumption of a uniform droplet concentration within the 6 × 410 m spray cloud. Since the deposit, like the dosage, is a time-integrated result, little change from that shown could be expected from the initial variations of concentration within the spray cloud alluded to earlier.

Overall, the model predicts that the top 4 m of the forest canopy collects about 14% of the deposited aminocarb. The model calculates that this height interval contains 9% of the foliage area (Belot et al. 1976) so that very little aminocarb could be expected to reach the ground through the remaining foliage.

III.3 ESTIMATE OF BYSTANDER EXPOSURE

III.3.1 DERMAL

The exposed area of a bystander's head and neck is first represented by a flat-plate normal to the droplet trajectories. For this worst-case calculation, the flat-plate geometry is adopted because it has a higher droplet interception efficiency than cylindrical or spherical geometry. The exposed area of the head and neck is known to be about 1300 cm^2 (Snyder et al. 1974) but the effective interception

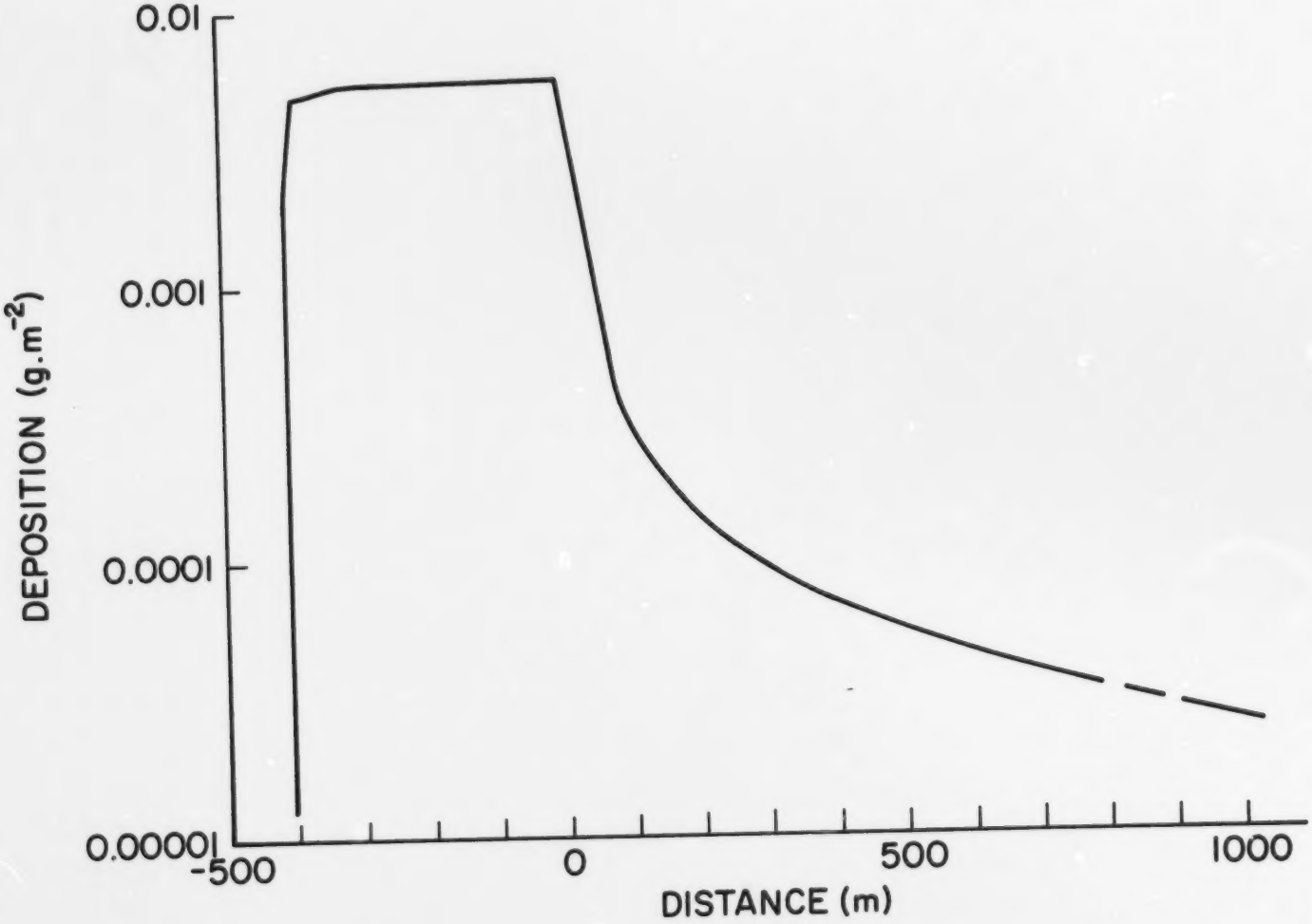

Figure III-1. Model-predicted deposition of aminocarb from an aerial spray of 70 g-AI.ha^{-1} (Crabbe 1982).

area to droplets would be less, possibly only one-half as much. A figure of 1000 cm^2 is adopted giving a flat plate 50 cm long and 20 cm wide, as 20 cm is the approximate overall width of the head.

The total exposed area of the hands and forearms, about 2400 cm^2 (based on Snyder et al. 1974), is also represented by a flat plate. The dimensions of this plate are 200 cm long by 9 cm wide, on the grounds that the effective interception area would be less than 2400 cm^2, and 9 cm is a representative width of the hands and forearms.

The effective droplet approach velocity is now assumed to be the vector sum of its terminal velocity and the mean wind speed, to reflect the fact that the dermal exposure is partly sedimentary deposition and partly by inertial impaction. The approach velocity will thus vary with the droplet diameter. The mean wind speed used in this calculation is the model wind speed at tree height, 50 $cm.s^{-1}$, inasmuch as this is the height where the highest atmospheric concentrations of droplets are predicted to occur in the forest. The resultant effective droplet velocity, V, is tabulated (Table III-2) in terms of its magnitude and mean angle to the horizontal.

Sample calculation:

The impact, or interception or collection efficiency, is a function of two dimensionless parameters, κ and Φ:

$$\kappa = \frac{D^2 V}{18(\partial_A/\partial_D)\,\gamma_A b}$$

$$\Phi = \frac{18\,bV}{(\partial_D/\partial_A)\,\gamma_A}$$

where: b = equivalent plate half width (cm)
∂_A = air density = 0.00127 $g.cm^{-3}$ at 5°C
∂_D = droplet density = 0.87 $g.cm^{-3}$ at the spray line
γ_A = air kinematic viscosity = 0.137 $cm^2.s^{-1}$ at 5°C
D = droplet diameter (μm)

Thus, for a 200 μm droplet, κ = 0.87 and Φ = 140 for the head and neck, and κ = 1.9 and Φ = 65 for the hands and forearms. Referring to Langmuir (1945), the collection efficiencies are therefore 55% and 74% respectively. Similar calculations may be performed for other droplet diameters.

The dermal exposure during cloud passage, of a bystander x m downwind from the spray line, may now be computed from the following expression:

$$E\,(x) = 2bl\,(Q/\delta Q) \int_0^\infty I(T,Do)\,(dm/dDo)dDo$$

Table III-2. Droplet velocities in terms of their magnitude and angle to the horizontal.

Droplet diameter D (μm)	Terminal velocity ($cm.s^{-1}$)	Effective droplet velocity V ($cm.s^{-1}$)	Angle (degrees)
25	1.7	50.0	1.9
50	6.6	50.4	7.5
75	14.1	52.0	15.7
100	23.3	55.2	25.0
150	43.6	66.3	41.1
200	63.4	80.7	51.8
250	83.6	97.4	59.1

where: E = exposure (g)

T = cloud residence time (s)

$I(T,Do) = \int_0^T C\ (Do, x, t)V\ (D(t))\ \lambda\ (D(t))\ dt$

V = effective droplet velocity

C(Do) = model concentration of droplets of diameter Do ($g.cm^{-3}$)

$\lambda(D)$ = collection efficiency at droplet diameter D

t = time (s)

l = equivalent plate length (cm)

b = equivalent plate half width (cm)

Q = source strength in g of aminocarb per metre of flight line
= $2.87\ g.m^{-2}$

δQ = initial model mass of aminocarb at diameter Do

dm/dDo = fraction of the initial aminocarb spray mass at diameter Do, such that $\int_0^\infty (dm/dDo)\ dDo = 1$

At the spray line, the time integral I(T) is simplified by assuming V, D and λ to be stationary. Downwind of the spray line, the time variation of D during cloud passage should be accounted for. In the numerical integration, a constant but more representative value of D, its value when C peaked, was actually used on the grounds that D varies only slowly during cloud passage and the maximum contribution to E occurs approximately as C peaks.

Numerical computation of E at the spray line yields the following dermal exposures, from a single swath, for an unprotected bystander:

0.47 mg for a treetop wind speed of 50 $cm.s^{-1}$
1.27 mg " " " " " " 100 $cm.s^{-1}$.

The exposures from a single swath, for a 70 kg man, at the spray line are therefore 6.72×10^{-3} and 1.81×10^{-2} $mg.kg\text{-}BW^{-1}$ respectively. The dermal exposure will continue to increase with wind speed to a theoretical maximum of 134 mg, i.e., all the aminocarb in a tube of 2800 cm^2 cross section area, 410 m long. However, this situation would never be realized in practice as it requires hypersonic atmospheric wind speed.

The value of I(T) in the above computations is approximately proportional to the time-integrated concentration or dosage, $\int_0^T C dt$, since V and λ vary only slowly with time during the exposure period. Model-predicted values of $\int_0^T C dt$, integrated over the droplet spectrum, are tabulated in Table III-3.

The effect of additional spray swaths, spaced upwind at 400 m intervals, is to increase the exposure slightly at any station downwind. The exposure will not simply be proportional to the sum of the time-integrated concentrations at 0, 400 and 800 m, etc. downwind of a single swath, but will also depend on the change in droplet size distribution with downwind distance.

Using the above method, the predicted dermal exposure for an unprotected bystander 400 m or 800 m downwind from a single swath is 3 x 10^{-6} or ~ 0 mg.kg-BW^{-1} respectively, in light winds. Thus the exposure for a bystander at the downwind edge of a multiswath spray block would not be significantly different from that due to a single swath in light 50 cm.s^{-1} winds. In 100 cm.s^{-1} winds the exposure from multiple swaths would be 1.84 x 10^{-2} mg.kg-BW^{-1}, a slight increase over the single swath exposure.

The computer model does not calculate the subcanopy atmospheric concentration of aminocarb. However, it will be less than the treetop values as is evidenced by the field data of Crabbe et al. (1980a). Here, the measured subcanopy dosage of fenitrothion from an aerial spray of 210 g-AI.ha^{-1} was 4.5 x 10^{-9} g.s.cm^{-3} compared to the present model-predicted treetop dosage of 2.7 x 10^{-8} g.s.cm^{-3} from matacil spray of 70 g-AI.ha^{-1}. Thus the subcanopy aminocarb dosage is expected to be about 1.5 x 10^{-9} g.s.cm^{-3} or 6% of the model-predicted treetop dosage. On this basis, the estimated total dermal exposure of a sheltered bystander would be about 0.5 µg.kg-BW^{-1}.

III.3.2 INHALATION

The sum of the time-integrated concentrations from multiple swaths, at a downwind edge of a spray block, in 50 cm.s^{-1} winds, is 2.7 x 10^{-8} g.s.cm^{-3}, a result obtained by extending the data of Table III-3 to account for the remainder of the swaths in a multi-swath operation. The inhalation exposure from droplets smaller than 5 µm diameter, which are assumed to contain less than 0.5% of the spray mass, is thus predicted to be 0.005 x 2.7 x 10^{-8} x 29000/60 or 9.3 x 10^{-7} mg.kg-BW^{-1} for a 70 kg subject breathing at 29 L.min^{-1}. At treetop winds of 100 cm.s^{-1}, the predicted inhalation exposure is reduced to 6.6 x 10^{-7} mg.kg-BW^{-1}. In the case of single swath the predicted exposures would be 8.5 x 10^{-7} and 5.9 x 10^{-7} mg.kg-BW^{-1} respectively.

The exposure for a bystander protected by the forest canopy would be about 6% of the above values.

Table III-3. Predicted treetop aminocarb dosage ($g.s.cm^{-3}$) from an aerial spray swath.

Treetop wind speed[α] ($cm.s^{-1}$)	Dosage ($g.s.cm^{-3}$) Distance from spray line, x(m)		
	0	400	800
50	2.47×10^{-8}	1.00×10^{-9}	4.62×10^{-10}
100	1.71×10^{-8}	9.60×10^{-10}	5.14×10^{-10}

[α] At a treetop wind speed of 50 $cm.s^{-1}$, the dosages equal the areas under the curves marked x = 0 m and x = 400 m in Figure 3-2.

III.3.3 ORAL

The oral exposure arises from droplets between 5 and 50 µm diameter which contain 7% of the spray mass (Figure 3-2). Thus the predicted oral exposure for an unprotected bystander at a spray line would be $0.07 \times 2.7 \times 10^{-8} \times 29000/60$ or 1.3×10^{-5} mg.kg-BW^{-1}, in light winds. Doubling the wind speed to 100 cm.s^{-1} reduces this exposure to 9.2×10^{-6} mg.kg-BW^{-1}.

III.4 MODEL PERFORMANCE

In a conference paper (Crabbe and Reid 1980), the percent active ingredient remaining airborne with distance from an aqueous fenitrothion aerial spray, predicted by the present model, compared favorably with a random-walk model of turbulence. In that comparison, the predicted percent airborne at 80 km was 0.21% from the present model and 0.12% from the random-walk model. Subsequent calculations showed that model predictions of the airborne aerosol concentration at 80 km were within 10% of each other. Also, when compared with the percent of airborne active ingredient measured during the 1979 N.B. field trials (Crabbe et al. 1980b) both models showed favorably. Further field validation will be undertaken soon (Crabbe et al. 1982).

III.4.1 GAPS IN KNOWLEDGE

It will be apparent to the reader that the chief gaps in knowledge in the model is the location of the spray cloud when the vortices dissipate. Careful theoretical and field studies are required to remove this uncertainty because modelling tests (e.g. Picot and Kristmanson 1980) show that initial source height has a strong influence on wind-borne drift. The interaction of the aircraft vortices with the forest environment is central to this problem so that any theoretical treatment would have to include the nonconservative drag forces exerted on the circulating flow by the trees as well as the fluid mechanics of the concentrated vorticity field in a turbulent atmosphere. Bilanin et al. (1978) have made a promising start by their analysis of this problem for the case of smooth ground. What is required now is extension of their analysis to the forest.

Another unknown is the initial droplet size distribution below 30 µm diameter. The present model extrapolated the measured distributions of Tomney et al. (1978) for diameters of 30 µm down to 0 µm. Field data (e.g. Picot et al. 1980) indicate abnormally large numbers of droplets below 30 µm diameter in aerial sprays. Plans are underway in Canada to measure the missing part of the droplet spectrum with laser Doppler interferometry.

Appendix IV. TOXICITY OF AMINOCARB FLOWABLE TO LABORATORY MAMMALS
(This data is included without critical review by the panel.)

Test	Response (95% CI)	Reference
	mg-AI.kg-BW^{-1}	
Acute Oral		
LD_{50} (male)	28.7 (25.4-32.6)$^{\alpha,\delta}$	Lamb et al. 1981a
LD_{50} (female)	31.4 (26.6-36.8)$^{\alpha,\delta}$	
NOEL	19.4$^{\alpha,\beta,\delta}$	
Acute Dermal[η]		
LD_{50}	582$^{\gamma,\delta}$	Lamb et al. 1981b
NOEL: Observed effect level	97: 194$^{\gamma,\delta,\zeta}$	
	µg-AI.L^{-1}.4 h^{-1}	
Acute Inhalation		
LD_{50}	155 (129-186)$^{\alpha,\varepsilon}$	Collins et al. 1981
	mg-AI.kg-BW^{-1}.d^{-1}	
Subacute Dermal 21-d exposure		
NOEL: Observed effect level;		Hixson 1981
local irritation	15.5$^{\gamma}$	
cholinesterase inhibition	15.5: 77.6$^{\gamma}$	
body weight	77.6: 388$^{\gamma}$	
gross-pathology or biochemistry	388	

α Rats.

β Symptoms included muscle fasciculations, tremors, ataxia, decreased activity, salivation, lacrimation exophthalmos, diarrhea, piloerection, unthrifty appearance and urine stain.

γ Rabbits.

δ Formulations was Matacil 180 Oil Flowable.

REFERENCES

Abdel-Wahab, A.M. 1971. Stability of two carbonyl-^{14}C-labelled methylcarbamate insecticides in some organic solvents. Bull. Entomol. Soc. Egypt Econ. Ser. 5: 27-31.

Abdel-Wahab, A.M. and Casida, J.E. 1967. Photooxidation of two 4-Dimethylaminoaryl methylcarbamate insecticides (Zectran and Matacil) on bean foliage and of alkylaminophenyl methylcarbamates on silica gel chromatoplates. J. Agric. Food Chem. 15: 479-487.

Abdel-Wahab, A.M., Kuhr, R.J. and Casida, J.E. 1966. Fate of C^{14}-carbonyl-labelled insecticide chemicals in and on bean plants. J. Agric. Food Chem. 14: 290-298.

Abou-Donia, M.B. and Graham, D.G. 1978. Delayed neurotoxicity of O-ethyl-O-4-nitrophenyl phosphenothioate: subchronic (90 days) oral administration in hens. Toxicol. Appl. Pharamcol. 45: 685-700.

Abou-Donia, M.B. and Graham, D.G. 1979. Delayed neurotoxicity of subchronic oral administration of leptophos to hens: recovery during four months after exposure. J. Toxicol. Environ. Health. 5: 1133-1147.

Abou-Donia, M.B. and Menzel, O.B. 1967. Fish brain cholinesterase: its inhibition by carbamates and automatic assay. Comp. Biochem. Physiol. 21: 99-108.

Addison, J.B. 1978. Application of Huckel Molecular Orbital Theory of the photodecomposition of pesticidal N-methylcarbamates. Chemosphere 12: 957-965.

Addison, J.B. 1981a. Vapour phase photochemistry of fenitrothion and aminocarb. Bull. Environ. Contam. Toxicol. 27: 250-255.

Addison, J.B. 1981b. Measurement of vapour pressures of fenitrothion and Matacil. Chemosphere 10: 355-364.

Addison, J.B., Silk, P.J. and Unger, I. 1974. The photochemical reactions of carbamates. II. The solution photochemistry of Matacil (4-dimethylamino-m-tolyl-N-methylcarbamate) and Landrin (2,3,5-trimethylphenyl-N-methylcarbamate). Bull. Environ. Contam. Toxicol. 11: 250-255.

Agriculture Canada. 1978. Proposed specifications insecticide diluent -585. Agriculture Canada, Ottawa.

Ahern, A. 1980. Mesures biologiques de l'impact du Matacil 1.4 OSC en eaux courantes. Report by Bio-Conseil Inc., Quebec. 151 pp.

Ahern, A. and Leclerc. 1981. Étude comparative des effets du Matacil et de fénitrothion sur les populations benthiques en eaux courantes. Rep. Bio-conseil Inc., Québec. 181 pp.

Albertini, A.V., Gross, D. and Zinn, M.W. 1968. Triaryl-phosphate poisoning in Morocco. 1959. Medical Book Corp., New York.

Aldridge, W.N. 1976. Reaction of swine esterases relevant to delayed neurotoxicity problems. In Pesticide induced delayed neurotoxicity problems. EPA 600/1-76-025. pp. 24-50.

Aldridge, W.N. and Reiner, E. 1972. Enzyme inhibitors as substrates. Interactions of esterases with esters of organophosphorus and carbamic acids. Elsevier Publ. Co., N.Y.

Anderson, L.D., Bay, E.C. and Mulla, M.S. 1965. Aquatic midge investigations in southern California. In California Mosquito Central Assoc. 33rd Conference Proceedings. pp. 31-33.

Anon. 1979. Environmental monitoring of the spruce budworm spray program in Newfoundland: final report. Nfld. Dept. Consumer Affairs and Environment. Inf. Report RA-80-1.

Applegarth, D.A., MacLeod, P.M., Toove, J.R., Kirby, L.T. and MacLaren, J.R. 1979. Organic acids and Reye's syndrome. Lancet 1: 1147.

Aprille, J.R. and Asimakis, G.K. 1979. A pathogenic role for a serum factor in Reye's syndrome. In Reye's syndrome II. Edited by J.F.S. Crocker. Grune and Stratton, New York. pp. 361-383.

Aprille, J.R., Austin, J., Costello, C.E. and Royal, N. 1980. Identification of the Reye's syndrome serum factor. Biochem. Biophys. Res. Commun. 94: 381-389.

Armson, K.A. 1977. Forest soils: properties and processers. Univ. of Toronto Press, Toronto.

Armstrong, J.A. 1981. Data supplied to the Panel. Forest Pest Management Institute.

Armstrong, J.A. and Kingsbury, P.D. 1979. Field evaluation of the environmental impact of nonyl phenol. Forest Pest Management Institute. Interm Progress Report. 62 pp.

Armstrong, J.A. and Yule, W.N. 1978. The distribution of aerially applied spray deposits in spruce trees. Can. Entomol. 110: 1259-1267.

Atwell, S.H. 1978. Soil adsorption and desorption of ^{14}C-Matacil. Mobay Chem. Corp. Report 66424.

Augenstein, L.L., McPhaul, L. and Wargo, J.P. 1978. Photodegradation of ^{14}C-Matacil on a soil surface. Mobay Chem. Corp. Report 50446.

Bagdon, R.E. and DuBois, K.P. 1956. Toxicity and pharmacologic effects of dimethylcarbamyl diethylthiocarbamyl sulfide. Arch. Int. Pharmacodyn. Ther. 108: 227-237.

Bagnell, P.C., Crocker, J.F.S and Ozere, R.L. 1978. Reye's syndrome in Canada's maritime provinces. Chemosphere 7: 565-571.

Balba, M.H. and Casida, J.E. 1968. Synthesis of possible metabolites of methylcarbamate insecticide chemicals substituted-aryl N-hydroxymethylcarbamates. J. Agric. Food Chem. 16: 821-825.

Balba, M.H. and Saha, J.G. 1974. Degradation of Matacil by the ascorbic acid oxidation system. Bull. Environ. Contam. Toxicol. 11: 193-200.

Barnes, D.H. 1979. 1978 Environmental monitoring of the spruce budworm spray program in Newfoundland. Nfld. Dept. Consumer Affairs and Environment. Inf. Report RA-79-2.

Barnes, D.H. 1980. 1979 Environmental monitoring spruce budworm spray program in Newfoundland. Nfld. Dept. Consumer Affairs and Environment. Inf. Report RA-80-1.

Baron, R.L., Casterline, J.L. and Fitzhugh, O.G. 1963. Specificity of carbamate-induced esterase inhibition in mice. Mobay Chem. Corp. Report 14292.

Baron, R.L., Casterline, J.L. and Fitzhugh, O.G. 1964. Specificity of carbamate-induced esterase inhibition in mice. Toxicol. Appl. Pharmacol. 6: 402-410.

Baskerville, G. (Task-Force Leader) 1976. Report of the task force for evaluation of budworm control alternatives. Prepared for The Cabinet Committee on Economic Development, Province of New Brunswick.

Belot, Y., Baille, A. and Delmas, J.L. 1976. Modele numerique de dispersion des polluants atmospheriques en presence de couverts vegetaux. Atmos. Environ. 10: 89-98.

Berger, M., Hart, S.S. and Roy, O.Z. 1970. Respiration, oxygen consumption and heart rate in some birds during rest and flight. Z. Vrgl. Physiol. 66: 201-204.

Berman, W., Pizzi, F., Schut, L., Raphaeli, R. and Holtzapple, P. 1975. The effects of exchange transfusion on intracranial pressure with Reye syndrome. J. Pediatr. 87: 887-891.

Bider, J.R. and Bracher, G.A. 1980. The effect of an experimental spraying of aminocarb on the activity of populations of terrestrial animals. Rept. de Ministère de l'Energie et des Resources, Gouvernement du Québec.

Bilanin, A.J., Teske, M.E. and Hirsh, J.E. 1978. The role of atmospheric shear, turbulence, and a ground plane in the dissipation of aircraft vortex wakes. Proc. of the American Institute of Aeronautics and Astronautics 16th Aerospace Sciences Meeting. Huntsville, Alabama. pp. 78-110.

Blevins, R.D., Lee, M. and Regan, J.D. 1977a. Mutagenicity screening of five methylcarbamate insecticides and their nitroso derivatives using mutants of Salmonella typhimurium LT2. Mutat. Res. 56: 1-6.

Blevins, R.D., Lijkinsky, W. and Regan, J.D. 1977b. Nitrosated methylcarbamate insecticides: effect on the DNA of human cells. Mutat. Res. 44: 1-7.

Bligh, E.G. and Dyer, W.J. 1959. A rapid method of total lipid extraction and purification. Can. J. Biochem. Physiol. 37: 911-917.

Bouldin, T.W. and Cavanagh, J.B. 1979. Organophosphorus neurapathy. I. A treated fiber study of the opatio-temporal spread of axonal degeneration. Am. J. Pathol. 94: 241-248.

Bove, K.E., McAdams, A.J., Partin, J.C., Partin, J.S., Hug, G. and Schubert, W.K. 1975. The hepatic lesion in Reye's syndrome. Gastroenterology 69: 685-697.

Brown, H.L. (undated). Non-target effects of Matacil sprayed for the control of spruce budworm in Maine. Mobay Chem. Corp. Report 66930.

Brown, H.L. 1978. Experience with aminocarb in Maine: efficacy and non-target effects. In Proc. Symp. on Aminocarb - Effects of its use on environmental quality. Edited by V.N. Mallet. University of Moncton, N.B. pp. 49-62.

Brun, G.L. and MacDonald, R.M. 1978. Analysis of aminocarb in water and sediments by gas liquid chromatography and high performance liquid chromatography. In Proc. Symp. on Aminocarb - Effects of its use on environmental quality. Edited by V.N. Mallet. University of Moncton, N.B. pp. 12-30 (cf. Bull. Environ. Contam. Toxicol. 24: 886-893).

Brun, G.L. and MacDonald, R.M. 1981. Nonyl phenol. Analytical methods manual. Water Quality Branch, Dept of Environ., Ottawa.

Buckner, C.H. and McLeod, B.B. 1977a. Ecological impact studies of experimental and operational spruce budworm (Choristoneura fumiferana Clem) control programs on selected non-target organisms in Quebec 1976. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-137.

Buckner, C.H. and McLeod, B.B. 1977b. Impact of experimental spruce budworm (Choristoneura fumiferana Clem) suppression trials upon forest dwelling birds in Newfoundland in 1977. Forest Pest Management Inst. Inf. Report FPM-X-9.

Buckner, C.H. and Sarrazin, R. 1975. Studies on the environmental impact of the 1974 spruce budworm control operation in Quebec. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-93.

Buckner, C.H. and McLeod, B.B and Ray, D.G.H. 1973. The effect of operational application of various insecticides on small forest birds and mammals. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-43.

Buckner, C.H., McLeod, B.B. and Kingsbury, P.D. 1975. Studies on the impact of the carbamate insecticide Matacil on components of forest ecosystems. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-91.

Buckner, C.H., McLeod, B.B. and Lidstone, R.G. 1976. Environmental impact studies of spruce budworm (Choristoneura fumiferana Clem) control programs in New Brunswick, 1976. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-135.

Busby, D.G., Pearce, P.A. and Garrity, N.R. 1982. Brain cholinesterase inhibition in forest passerines exposed to experimental aminocarb spraying. Bull. Environ. Contam. Toxicol. (In press)

Butler, P.A. 1962. Effect of Bayer 44646 on oysters. Mobay Chem. Corp. Report 11106B.

Canadian Forestry Service. 1981. Data extracted from reports of the Annual Forest Pest Control Forum.

Carl, M. 1978. Internal laboratory quality control in the routine determination of chlorinated pesticide residues. In Advances in pesticide science, plenary lectures and symposia papers. Edited by H. Geissbuehler. Pergamon Press, Oxford. pp. 660-663.

Carpenter, C.P., Weil, C.S., Palm, P.E., Woodside, M.W., Nair, J.H. and Smyth, H.F. 1961. Mammalian toxicity of 1-naphthyl-N-methylcarbamate (Sevin insecticide). J. Agric. Food Chem. 9: 30-39.

Carrow, J.R. 1974. Aerial spraying operations against black-headed budworm on Vancouver Island-1973. Pacific Forest Research Centre. Inf. Report BC-X-101. 56 pp.

Carrow, J.R., Nicholson, S.A. and Howse, G.M. 1980. Spruce budworm spraying in Ontario 1979. Forest Resources Branch, Ont. Ministry of Natural Resources. Pest Control Report No. 8.

Carter, N.E. 1979. The 1977, 1978 aerial forest protection program against spruce budworm in Newfoundland. Dept. of Forestry. Inf. Rep. FP-2.

Casida, J.E. 1963. Mode of action of carbamates. Ann. Rev. Entomol. 8: 39-58.

Casida, J.E. and Baron, R.L. 1976. Recognition and overview of the organophosphorus induced delayed neurotoxicity problem. In Pesticide induced delayed neurotoxicity. EPA 600/1-76-025. pp. 7-23.

Cavanagh, J.B. 1973. Peripheral neutopathy caused by chemical agents. CRC Rev. Toxicol. 2: 365-417.

CDC. 1982. National surveillance for Reye's syndrome, 1981: update, Reye's syndrome and salicylate usage. Centre for Disease Control. Morbidity and Mortality Weekly. Rep. 31: 53-61.

Chutter, F.M. 1972. A reappraisal of Needham and Usinger data on the variability of stream fauna when sampled with a Surber sampler. Limnol. Oceanogr. 17: 139-141.

Chutter, F.M. and Noble, R.G. 1966. The reliability of a method of sampling stream invertebrates. Arch. Hydrobiol. 62: 95-103.

Chaves-Carballo, E., Carter, G.A. and Wiebe, D.A. 1979. Triglyceride and cholesterol concentrations in whole serum and in serum lipoproteins in Reye's syndrome. Pediatrics 64: 592-597.

Ch'ien, L., Belluomini, J., and Lemmi, H. 1979. Visual evoked potentials in Reye's syndrome. Clin. Encephalogr. 10: 164-167.

Chiou, C.T., Freed, V.H., Schmedding, D.W. and Kohnert, R.L. 1977. Partition coefficient and bioaccumulation of selected organic chemicals. Environ. Sci. Technol. 11: 475-478.

Christofferson, P., Faarup, P., Geertinger, P. and Krough, P. 1980. Reye's syndrome in a child on long-term salicylate medication. Forensic Sci. 15: 129-133.

Coady, L.W. 1978. Immediate chemical and toxicological influences of aerially applied fenitrothion and aminocarb in selected Newfoundland streams. Canada Dept. of Environment. Surveillance Report EPS-5-AR-78-1.

Collins, C.J., Lulham, G., Breckenridge, C.B., Losos, D.V.M., Broxup, B.R. and Procter, D.V.M. 1981. The acute toxicity of inhaled Matacil formulation in the albino rat. Mobay Chem. Corp. Report 80365.

Corey, L., Rubin, R., Hattwick, M., Noble, G. and Cassidy, E. 1976. A nationwide outbreak of Reye's syndrome: Its epidemiologic relationship to influenza B. Am. J. Med. 61: 615-625.

Corey, L., Rubin, R.J. and Hattwick, M.A.W. 1977. Reye's syndrome: Clinical progression and evaluation of therapy. Pediatrics 60: 708-714.

Couture, P., Lambert, M. and Visser, S.A. 1979. Effets toxique des insecticides fenitrothion et Matacil sur le phytoplancton et le zooplancton. INRS-Eau, Université de Quebec, Ste. Foy. Rapp. SRI 102.

Crabbe, R. 1982. Data submitted to Panel. National Research Council Canada, Ottawa.

Crabbe, R.S. and Reid, J.D. 1980. Results from two models for the long-distance drift and dry deposition of an insecticide cloud onto a forest. AMS, APCA Second Joint Conference on Applications of Air Pollution Meteorology, New Orleans. March 24-27, 1980.

Crabbe, R., Krzymien, M., Elias, L. and Davie, S. 1980a. New Brunswick spray operations: measurement of atmospheric fenitrothion concentrations near the spray area. National Research Council Canada. Report No. LTR-UA-56.

Crabbe, R., Elias, L., Krzymien, M. and Davie, S. 1980b. New Brunswick forestry spray operations: field study of the effect of atmospheric stability on long-range pesticide drift. National Research Council Canada. Report No. LTR-UA-52.

Crabbe, R., Krzymien, M., Elias, L. and Davie, S. 1982. Field study of effect of atmospheric stability on target deposition and effective swath widths for aerial forest sprays in New Brunswick. Part I. National Research Council Canada. Report No. LTR-UA-62.

Crawford, C.R. and Anderson, R.H. 1972a. The acute oral toxicity of Matacil 1.4 OSC undiluted and diluted with diesel oil to rats. Mobay Chem. Corp. Report 35000.

Crawford, C.R. and Anderson, R.H. 1972b. The acute oral toxicity of Matacil 1.4 oil soluble concentrate undiluted and diluted with diesel oil to rats. Mobay Chem. Corp. Report 33111.

Crocker, J.F.S. and Bagnell, P.C. 1981. Reye's syndrome: a clinical review. Can. Med. Assoc. J. 124: 375-382.

Crocker, J.F.S., Ozire, R.L., Rozie, K.R., Digout, S.C. and Hutzinger, O. 1976. Lethal interaction of ubiquitous insecticide carriers with virus. Science 192: 1351-1353.

Crocker, J.F.S., Rozee, K.R., Renton, K.W. and Lee, S.H.S. 1981. An experimental model of Reye's syndrome chemical and influenza B virus interaction. Pediatr. Res. 15: 530.

Crosby, D.G., Leitis, E. and Winterlin, W.L. 1965. Photodecomposition of carbamate insecticides. J. Agric. Food Chem. 13: 204-207.

DeBoo, R.F. and Hildahl, V. 1967. Aerial spraying for control of the jackpine budworm in Manitoba. Manit. Entomol. 1: 21-26.

Decino, T.J. 1963. Toxicity of Bayer 44646 to birds. Mobay Chem. Corp. Report 10532. 12 pp.

Desaulniers, R. 1977. Comparaison des programmes de traitement des forêts réalisés au Québec et au Nouveau Brunswick. In Fenitrothion: the long-term effects of its use in forest ecosystems. Edited by J.R. Roberts, R. Greenhalgh and W.D. Marshall. National Research Council Canada. NRCC No. 16073.

DeVivo, D.C. 1978. Reye's syndrome: a metabolic response to an acute mitochondrial insult? Neurology (Minneap). 28: 105-8.

DeVivo, D.C., Keating, J.P. and Haymond, M.W. 1975. Reye's syndrome: Results of intensive supportive care. J. Pediatr. 87: 875-880.

Dilley, J. and Doull, J. 1962. The acute inhalation toxicity of Bayer 44646 to rats and mice. Mobay Chem. Corp. Report 9413.

Dorigan, J., Fuller, B. and Duffy, R. 1976. Preliminary scoring of selected organic air pollutants, Appendix III. Prepared for the Environmental Protection Agency, October 1976. PB 264445.

Douglas, G. 1982. Data submitted to Panel. Health and Welfare Canada, Ottawa.

Doull, J. and Root, M. 1963. Subacute oral toxicity of Bayer 44646 in male and female dogs. Mobay Chem. Corp. Report 12267.

Doull, J., Root, M. and Meskauskas, J. 1967. Chronic oral toxicity of Bay 44646 to rats. Mobay Chem. Corp. Report 21172.

DuBois, K.P. 1962. The acute oral toxicity of Bayer 44646 to chickens. Mobay Chem. Corp. Report 9422.

DuBois, K.P. 1963. The acute toxicity of some possible metabolites of Bay 39007, 44646, 37344 and Morestan. Mobay Chem. Corp. Report 12379.

DuBois, K.P. 1968. The acute oral, dermal and inhalation toxicity of a Matacil formulation. Mobay Chem. Corp. Report 22664.

DuBois, K.P. and Kinoshita, F. 1962. The subacute parenteral toxicity of Bayer 44646 to female rats. Mobay Chem. Corp. Report 9754.

DuBois, K.P., and Kinoshita, F. 1965. Inability of Baygon and Bayer 44646 to induce synthesis of microsomal detoxification enzymes. Mobay Chem. Corp. Report 16572.

DuBois, K.P. and Raymund, A.B. 1962a. The acute toxicity of Bayer 44646 formulations to rats. Mobay Chem. Corp. Report 9409.

DuBois, K.P. and Raymund, A.B. 1962b. The acute toxicity of Bayer 44646 to mammals. Mobay Chem. Corp. Report 8308.

DuBois, K.P. and Raymund, A.B. 1962c. The acute toxicity of Bayer 44646 in combination with other anticholinesterase insecticides. Mobay Chem. Corp. Report 10241.

DuBois, K.P., Doull, J., Vesselinovitch, D. and Niskauskas, J. (undated). The dermal toxicity of a wettable powder of Bayer 44646 applied repeatedly to the skin of rats. Mobay Chem. Corp. Report 14250.

Egert, G. and Greim, H. 1976. Formation of mutagenic N-nitroso compounds from the pesticides Biomotryne, Dodine and Carbaryl in the presence of nitrite at pH 1. Mutat. Res. 37: 179-186.

Eidt, D.C. 1978. Penetration of fenitrothion and aminocarb into stream gravel and effects on benthic insects. In Environmental surveillance of insecticide spray operations in New Brunswick budworm infested forests - 1977. Edited by I.W. Varty. Maritimes Forest Research Centre. Inf. Report M-X-87. pp. 8-9.

Eidt, D.C. 1979. Toxicity of aminocarb to insects in a woodland stream. Maritimes Forest Research Centre. Inf. Report M-X-96.

Eidt, D.C. 1980a. The toxicity of aminocarb and fenitrothion to stream insects. In Environmental surveillance in New Brunswick 1978-1979: Effects of spray operations for forest protection. Edited by I.W. Varty. University of New Brunswick, N.B. pp. 52-53.

Eidt, D.C. 1980b. The effects of fenitrothion and aminocarb on growth of aquatic decomposition fungi. In Environmental surveillance in New Brunswick 1978-1979: Effects of spray operations for forest protection. Edited by I.W. Varty. University of New Brunswick, N.B. p. 53.

Eidt, D.C. and Fisher, R.A. 1982. Frequency of forest spraying in New Brunswick. J. Can. For. Serv. Research Notes. (In press)

Eidt, D.C. and Sundaram, K.M.S. 1975. The insecticide fenitrothion in headwaters streams from large scale forest spraying. Can. Entomol. 107: 735-742.

Eidt, D.C., Salonius, P.O. and Meating, J.H. 1979. Effects of fenitrothion and aminocarb on aquatic decomposing fungi. Bi-Monthly Res. Notes Can. For. Serv. 35: 17-18.

Eidt, D.C., Salonius, P.O. and Meating, J.H. 1980. Effets du fenitrothion et de l'aminocarb sur les champignons de décomposition aquatiques. Rev. bimestnielle de Recherches 36: 5-6.

Elespuru, R., Lijinsky, W. and Setlow, J.K. 1974. Nitrosocarbaryl as a potent mutagen of environmental significance. Nature 247: 386-387.

Elner, J.K. and Wildish, D.J. 1981. Seasonal data on the microbial community of four New Brunswick ponds, including a period of experimental spraying with Matacil. Can. Tech. Rep. Fish Aquat. Sci. No. 993: 21 pp.

Elner, J.K., Wildish, D.J. and Johnston, D.W. 1981. Fate of sprayed formulated aminocarb in freshwater. Chemosphere 10: 1025-1034.

Elner, J.K., Wildish, D.J. and Johnston, D.W. 1982. Carbon-14 assimilation by algal communities of oligotrophic ponds treated wtih formulated aminocarb. Arch. Environ. Contam. Toxicol. (In press)

Environmental Monitoring Committee. 1979a. 1977 Environmental monitoring of the spruce budworm spray programs in Newfoundland. Nfld. Dept. Consumer Affairs and Environment. Inf. Report RA-79-1.

Environmental Monitoring Committee. 1979b. 1978 Environmental monitoring of the spruce budworm spray program in Newfoundland. Nfld. Dept. Consumer Affairs and Environment. Inf. Report RA-79-2.

Environmental Protection Service. 1981. Unpublished data received from W. Ernst, Environmental Protection Service, Halifax, N.S.

Ernst, W.R. 1981. Preliminary report of the acute toxicity of Matacil 1.8 F^{R}, its formulations and components to aquatic fauna. Report to the Canadian Forest Pest Control Forum 1981, Ottawa.

Ernst, W.R., Julien, G., Doe, K. and Parker, R. 1981. Environmental investigations of the 1980 spruce budworm spray programs in New Brunswick. Environmental Protection Service., Halifax, N.S. EPS-5-AR-81-3.

Estenik, J.F. and Collins, W.J. 1979. In vivo and in vitro studies of mixed-function oxidase in an aquatic insect, Chironomus riparius. ACS Symp. Ser. 99: 349-370.

Everett, L.J. 1965. Detection of Matacil exposure in plant personnel. Mobay Chem. Corp. Report 14504.

Faraj, B.A., Neuman, S.L., Caplan, D.B., Ali, F.M., Camp, V.M. and Ahmann, P.A. 1979. Evidence for hypertyraminemia in Reye's syndrome. Pediatrics 64: 76-80.

Federal Register. 1978. Proposed guidelines for registering pesticides in the U.S. Hazard evaluation: humans and domestic animals. Part II. Fed. Regist. 43(163): 37336-37403.

Federal Working Group on Pest Management. 1974. Occupational exposure to pesticides. Washington, D.C.

Finnegan, R.J. 1978. Predation by Formica lugubris on Choristoneura fumiferana. Bi-Mon. Res. Notes Can. For. Serv. 4: 3-4.

Flint, D.R. 1981. Information supplied to Panel. Mobay Chemical Corporation, Kansas City, Missouri.

Fowle, C.D. 1972. Effects of phosphamidon on forest birds in New Brunswick. Can. Wildl. Serv. Rep. Ser. 16.

Franklin, C.A., Muir, N.I. and Greenhalgh, R. 1981. The assessment of potential health hazards to orchardists spraying pesticides. In Pesticide residues and exposure. Edited by J.R. Plimmer. ACS Symposium Series 182: 157-168.

Friend, M. and Trainer, D.O. 1970. Polychlorinated biphenyl: interaction with duck hepatitis virus. Science 170: 1315.

Fullerton, P.M. and Barnes, J.M. 1966. Peripheral neuropathy in rats produced by acrylamide. Br. J. Ind. Med. 23: 210-221.

Gaboury, G. 1979. Environmental surveillance of aerial spraying against the spruce budworm in Quebec in 1979. Report to the Forest Pest Control Forum, 1979, Ottawa.

Gaboury, G. 1980. Surveillance environmentale des pulverisation arriennes 1979 contre la tordeuse des bourgeons de l'épinette au Québec. Rapp. Prélim. Sous-comité de l'environnement du Comité de surveillance écologique et de pathologie, Québec.

Gaines, T.B. 1969. Acute toxicity of pesticides. Mobay Chem. Corp. Report 25529.

Gaworski, C.L., Kinkead, E.R. and Doyle, R.L. 1979. Acute toxciity of a number of chemicals of interest to the air force. Report ISS AMRL-TR-79-11.

Germain, P. and Morin, G. 1979. Forest songbird population 1978 monitoring program in relation to aerial spray of insecticides against spruce budworm. New Brunswick Dept. of Natural Resources. Avifauna Ltd., Moncton, N.B. 31 pp.

Germain, P. and Tingley, S. 1980. Population responses of songbirds to 1979 forest spray operations in New Brunswick. Forest Protection Ltd. Avifauna Ltd., Moncton, N.B. 31 pp.

Gillis, G.F. 1978. Benthic drift. In Environmental surveillance of insecticide spray operation in New Brunswick's budworm infested forests - 1977. Edited by I.W. Varty. Maritimes Forest Research Centre. Inf. Report M-X-87. pp. 8.

Gosselin, R.E., Hodge, H.C., Smith, R.P. and Gleason, M.N. 1976. Clinical toxicology of commercial products. Acute Poisoning. Williams and Wilkins Co, Baltimore. pp. 1783.

Greenbank, D.O., Schaefer, G.W. and Rainey, R.C. 1980. Spruce budworm moth flight and dispersal: new understanding from canopy observations, radar and aircraft. Mem. Entomol. Soc. Can. 110: 1-49.

Guilbault, G.G., Lozes, R.L., Moore, W. and Kuan, S.S. 1972. Effects of pesticides on cholinesterase from aquatic species: crayfish, trout and fiddler crab. Environ. Lett. 3: 235-45.

Guyton, A.C. 1971. Basic human physiology: Normal function and mechanisms of disease. W.B. Saunders, Toronto.

Hall, R.J. and Kolbe, K. 1980. Bioconcentration of organophosphorus pesticides to hazardous levels by amphibians. J. Toxicol. Environ. Health 6: 853-860.

Hamel, D.R. 1977. The effects of Bacillus thuringiensis on parasitoids of the western spruce budworm, Choristoneura occidentalis, and the spruce coneworm Dioryctria reniculelloides in Montana. Can. Entomol. 109: 1409-1415.

Harris, C.R. 1981. Information supplied to Panel. Agriculture Canada, London, Ont.

Harris, C.R. and Svec, H.J. 1976. Onion maggot resistance to insecticides. J. Econ. Entomol. 69: 617-619.

Hart Chemical Limited. 1978. Safety data sheet on nonyl phenol. Guelph, Ontario.

Hattwick, M.A.W. and Sayetta, R.B. 1979. The trends of Reye's syndrome based on national statistics. In Reye's syndrome II. Edited by J.F.S. Crocker. Grune and Stratton, New York. pp. 13-32.

Hayes, W.T. 1975. Toxicology of pesticides. Williams and Wilkins Co., Baltimore.

Heyndricks, A. and Von Hoof, F. 1971. The acetylcholinesterase activity of carbamate pesticides upon plasma. Meded. Fac. Landbouwwet., Rijksuniv. Gent 39: 425-438.

Hixson, E.J. 1981. Subchronic 21-day dermal toxicity study on Matacil 180 oil flowable in rabbits. Mobay Chem. Corp. Report 80054.

Hill, E.F., Heath, R.G., Spann, J.W. and Williams, J.D. 1975. Lethal dietary toxicities of environmental pollutants to birds. U.S. Dept. Interior. Fish Wildlife Service Report 191.

Hilty, M.D., McClung, H.J., Haynes, R.E., Ramsle, C.A. and Sherard, E.S. 1979. Reye's syndrome in siblings. J. Pediatr. 94: 576-9.

Holmes, S.B. 1979. Aquatic impact studies of a spruce budworm control program in the lower St. Lawrence region of Quebec in 1978. Forest Pest Management Institute. Report FPM-X-26.

Holmes, S.B. 1981. Preliminary report comparing the effects of three formulations of Matacil insecticide on components of stream ecosystems. Forest Pest Management Institute. File Report No. 16.

Holmes, S.B. and Kingsbury, P.D. 1980. The environmental impact of nonyl phenol and the Matacil formulation. Part 1. Aquatic ecosystems. Forest Pest Management Institute. Report FPM-X-35.

Horowitz, W. 1981. Analytical aspects: an introduction. In The pesticide chemist and modern toxicology. Edited by S.K. Banbal, J.J. Marco, L. Golberg and M.L. Leng. ACS Symposium Series 1160, Washington. pp. 331-334.

Houghton, E.R. 1978. Standarized scenarios of pest control situations as a means of assessing human exposure to pesticides - occupational and environmental exposure. Control Products Section, Agriculture Canada, Ottawa.

Howard, K.A. 1982. Information supplied to Panel. Chemagro Ltd., Mississauga, Ont.

Howse, C.W., Hale, E.J. and Maguire, R.J. 1978. Analysis of environmental samples for constituents of an aromatic solvent used in fenitrothion spray formulations. Bull. Environ. Contam. Toxicol. 20: 751-759.

Huttenlocher, P.R. and Trauner, D.A. 1978. Reye's syndrome in infancy. Pediatrics 62: 84-90.

Huttenlocher, P.R., Schwartz, A.P. and Klatskin, G. 1969. Reye's syndrome: ammonia intoxication as a possible factor in the encephalopathy. Pediatrics 43: 443-454.

HWC. 1975. The testing of chemicals for carcinogenicity, mutagenicity, teratogenicity. Health and Welfare Canada, Ottawa.

IARC. 1976. Evaluation of carcinogenic risk of chemicals to humans. IARC Monograph 12: 11.

Ingebo, R.D. and Foster, H.H. 1957. Drop-size distribution for cross-current breakup of liquid jets in airstreams. NACA TN4087.

Jager, K.W. 1976. Organophosphate exposure from industrial usage, electroneuromyography in occupational medical supervision of exposed workers. In Pesticide induced delayed neurotoxicity. EPA 600/1-76-025. pp. 152-188.

Jefferson Chemical Company Inc. 1964. Data sheet for nonyl phenol.

Johnson, D.P. 1964. Determination of Sevin insecticide residues in fruit and vegetables. J. Assoc. Off. Anal. Chem. 47: 283-286.

Johnson, M.K. 1969a. A phosphorylation site in brain and the delayed neurotoxic effect of some organophosphorus compounds. Biochem. J. 111: 487-495.

Johnson, M.K. 1969b. The delayed neurotoxic effects of some organophosphorus compounds: identification of the phosphorylation site as an esterase. Biochem. J. 114: 711-717.

Johnson, M.K. 1970. Organophosphorus and other inhibitors of brain neurotoxic esterase and the development of delayed neurotoxicity in hens. Biochem. J. 120: 523-531.

Johnson, M.K. 1976. Mechanism of protection against the delayed neurotoxic effects of organophosphorus esters. Fed. Proc. 35: 73-74.

Johnson, M.K. 1980. Neurotoxicity: mechanism explored and exploited. Nature 287: 105-106.

Kang,E.S. 1979. Resolution of the presence of multiple forms of cyclic nucleotide phosphodiesterase (PDE) in normal and Reye's syndrome liver. Pediatr. Res. 13: 946-947.

Kenaga, E.E. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. Environ. Qual. Safety 2: 166-181.

Kettela, E.G. 1981. Information supplied to Panel. Maritimes Forest Research Centre, Fredericton, N.B.

Kimmerle, G. 1964. Matacil/5080a. Mobay Chem. Corp. Report 14135.

Kimmerle, G. 1965. Compound Heiss A-363. Mobay Chem. Corp. Report 16270.

Kingsbury, P.D. 1978. Aquatic impact studies by FPMI in Quebec spruce budworm spray block 305, 1977. Forest Pest Management Institute. Report FPM-X-12.

Kingsbury, P.D. and McLeod, B.B. 1978. Studies on the environmental impact of aminocarb on aquatic and terrestrial forest ecosystems. In Proc. Symp. Aminocarb - Effects of its use on environmental Quality. Edited by V.N. Mallet. Univ. of Moncton, N.B. pp. 105-117.

Kingsbury, P.D. and McLeod, B.B. 1979. The impact of the 1978 spruce budworm larvicide timing trials in Quebec upon forest avifauna. Forest Pest Management Institute. Inf. Report FPM-X-29.

Kingsbury, P.D. and McLeod, B.B. 1980. The impact of spruce budworm control projects involving sequential applications upon forest avifauna in the lower St. Lawrence region. Forest Pest Management Institute. Inf. Report FPM-X-34.

Kingsbury, P.D., McLeod, B.B. and Millikin, R.L. 1981a. The environmental impact of nonyl phenol and the Matacil formulation. Part 2: terrestrial ecosystems. Canada Forestry Service Report FPM-X-36.

Kingsbury, P.D., McLeod, B.B. and Mortenson, K.L. 1981b. Preliminary report on studies of the impact of Matacil formulations on honey bees and wild pollinators. Forest Pest Management Institute. File Report No. 18.

Klein, A.W., Harnisch, M., Poremski, H.J. and Schmidt-Bleek, F. 1981. OECD chemicals testing programme: physico-chemical tests. Chemosphere 10: 153-207.

Krishna, J.C. and Casida, J.E. 1966. Fate in rats of ten variously labelled methyl- dimethyl-carbamate-^{14}-C insecticide chemicals and their hydrolysis products. J. Agric. Food Chem. 14: 98-105.

Krucera, D.R., Orr, P.W. and Ford, R.P. 1976. Evaluation of the efficacy of Dylox, Matacil and Sumithion against the spruce budworm Choristoneura fumiferana (Cle) in Maine 1975. In Cooperative pilot control project of Dylox, Matacil and Sumithion for spruce budworm control in Maine. Forest Insect and Disease Management, U.S. Forest Service. pp. 75-87.

Kruckenburg, S.M. 1977. Acute oral toxicity of Matacil in chickens. Mobay Chem. Corp. Report 54381.

Kruckenburg, S.M. 1978. Delayed neurotoxicity study of Matacil in hens. Mobay Chem. Corp. Report 54380.

Kuhr, R.J. and Casida, J.E. 1967. Persistent glycosides of metabolites of methylcarbamate insecticide chemicals formed by hydroxylation in bean plants. J. Agric. Food Chem. 15: 814-824.

Kuhr, R.J. and Dorough, H.W. 1976. Carbamate insecticides: Chemistry and biochemistry. CRC Press Inc., Cleveland.

Lamb, D.W. 1981. Information supplied to panel. Mobay Chem. Corp., Kansas City, Missouri.

Lamb, D.W. and Jones, R.E. 1975. Acute and oral toxicity of Matacil technical to adult bobwhite quail and adult mallard ducks. Mobay Chem. Corp. Report 43810.

Lamb, D.W. and Roney, D.J. 1975. Acute toxicity of Matacil and four metabolites to bluegill and rainbow trout. Mobay Chem. Corp. Report 44208.

Lamb, D.W. and Roney, D.J. 1976. Accumulation and persistence of residues in channel catfish exposed to Matacil-^{14}C. Mobay Chem. Corp. Report 49309.

Lamb, D.W., Sherman, M.A. and Jones, R.E. 1978. Accumulation and elimination of residues in bobwhite quail exposed to Matacil-^{14}C. Mobay Chem. Corp. Report 49310.

Langmuir, I. 1945. Atmospheric phenomena. In The collected works of Irving Langmuir. Volume 10. 1961. Pergamon Press, Oxford.

Lamb, D.W., Hixson, E.J., English, T.D., Mallicoat, D.R. and Schroeder, R.S. 1981a. Acute oral toxicity of Matacil 180 oil flowable to rats. Mobay Chem. Corp. Report 69502.

Lamb, D.W., Hixson, E.J., English, T.D., Hoss, H.E., Mallicoat, D.R. and Schroeder, R.S. 1981b. Acute dermal toxicity of Matacil 180 oil flowable. Mobay Chem. Corp. Report 69961.

Lamb, D.W., Hixson, E.J., English, T.D., Mallicoat, D.R. and Schroeder, R.S. 1981c. Eye and dermal irritation of Matacil 180 oil flowable. Mobay Chem. Corp. Report 69602.

Lanouette, M. and Pike, R.K. 1980. Analysis of aminocarb formulations by high-performance liquid chromatography. J. Chromatogr. 190: 208-211.

Laperle, M. 1964. Inventaire du Lac Ste. Anne, Parc de la Gaspesie, 1964. Service de la Faune du Quebec. 10 pp.

Lawrence, J.F. 1976. Gas chromatographic analysis of heptafluorobutyryl derivatives of some carbamate insecticides. J. Chromatogr. 123: 287-292.

Lawrence, J.F. 1977. Direct analysis of some carbamate pesticides in foods by HPLC. J. Agric. Food Chem. 25: 211-212.

Lee, S.H.S., Laltoo, M., Crocker, J.F.S. and Rozee, K.R. 1980. Emulsifiers that enhance susceptibility to virus infection: increased virus penetration and reduced interferon response. Appl. Environ. Microbiol. 40: 787-793.

Lemieux, R. 1977. Projet de surveillance écologique arrosages aerriens (faune aquatique), dans le secteur du Parc Pêches Environnement Canada. Rapport preliminaire synthèse, St. Foy, Québec.

Leonard, S.H. 1979. Matacil: a summary of literature of environmental hazard, human health hazard, and efficacy in spruce budworm control. Dept. Entomol., Univ. of Maine.

Levesque, D. and Mallet, V.N. 1980. Gas liquid chromatographic analysis of aminocarb and seven derivatives. J. Chromatogr. 200: 228-233.

Lewis, F.B. 1960. Factors affecting assessment of parasitization by Apanteles fumiferanae and Glypta fumiferanae on spruce budworm larvae. Can. Entomol. 92: 881-891.

Li, M.F. 1981. Information supplied to Panel. Fisheries and Oceans, Resource Branch, Halifax, N.S.

Liddle, J.A., Kimbrough, R.D., Needham, L.L., Cline, R.E., Svrek, A.L., Yert, L.W. and Bayse, D.D. 1979. A fatal episode of accidental methomyl poisoning. Clin. Toxicol. 15: 159-167.

Lijinsky, W. and Elespuru, R. 1975. Mutagenicity and carcinogenicity of N-nitroso derivatives of carbamate insecticides. IARC Meeting National Tech. Inform Serv. Conf. 7510181-1.

Lijinsky, W. and Taylor, H.W. 1976. Carcinogenesis in Sprague-Dawley rats of N-nitroso-N-alkyl carbamate esters. Can. Lett. 1: 275-279.

Lijinsky, W. and Taylor, H.W. 1977. Transplacental chronic toxicity testing of carbaryl with nitrite in rats. Food Cosmet. Toxicol. 15: 229-232.

Linnemann, C.C., Kauffman, C.A., Shea, L. and Schiff, G.M. 1974. Association of Reye's syndrome with viral infection. Lancet 2: 179-182.

Lippman, M., Yeates, D.B., Albert, R.E. 1980. Deposition, retention and clearance of inhaled particles. Br. J. Ind. Med. 37: 337-362.

Lockhart, W.L., Metner, D.A. and Grift, N. 1973. Biochemical and residue studies in rainbow trout (Salmo gairdneri) following field and laboratory exposures to fenitrothion. Manit. Entomol. 7: 26-36.

Lotti, M. and Johnson, M.K. 1978. Neurotoxicity of organophosphorus pesticides: predictions can be based on in vitro studies with hen and human enzymes. Arch. Toxicol. 41: 215-221.

Lowe, J.I. 1962. Effects of pesticides on marine animals. Mobay Chem. Corp. Report 14804.

Lyons, D.B., Buckner, C.H., McLeod, B.B. and Sundaram, K.M.S. 1976. The effects of fenitrothion, Matacil and Orthene on frog larvae. Chem. Control Res. Inst., Ottawa. Inf. Rep. CC-X-129.

MacCallum, M.E. 1980. The short term environmental impact of the spruce budworm spray program in Ontario. Pest. Control Section, Ont. Ministry of Natural Resources.

Macdonald, D.R. and Webb, F.E. 1963. Insecticides and the spruce budworm. In The dynamics of epidemic spruce budworm populations. Edited by R.F. Morris. Mem. Entomol. Soc. Can. 31: 288-310.

Mackay, D. and Leinonen, P.J. 1975. Rate of evaporation of low solubility contaminants from water bodies to atmosphere. Environ. Sci. Technol. 9: 1178-1180.

Mackay, D., Bobra, A., Shiu, W.Y. and Yalkowsky, S.H. 1980. Relationships between aqueous solubility and octanol-water partition coefficients. Chemosphere 9: 701-711.

Mackenzie, C. 1962. Toxicity of Chemagro products to starfish. Mobay Chem. Corp. Report 11375.

Magasi, L.P. 1981. Data submitted to Panel. Maritimes Forest Research Centre, Fredericton, N.B.

Magasi, L.P., Titus, F.A. and Kettela, E.G. 1980. Parasitism and biological control. In Environment surveillance in New Brunswick 1978-79: effects of spray operations for forest protection against spruce budworm. Edited by I.W. Varty. University of New Brunswick, N.B. pp. 46-47.

Maguire, R.J. 1980. Pollutants in aquatic surface microlayers: A cautionary note. Int. J. Environ. Anal. Chem. 7: 253-255.

Maguire, R.J. and Hale, E.J. 1980. Fenitrothion sprayed on a pond: kinetics of its distribution and transformation in water and sediment. J. Agric. Food Chem. 28: 372-378.

Mamarbachi, G. 1978. Recherche et dosage des residues d'aminocarb dans l'environnement forestier par chromatographie en phase gazeuse. In Proc. symp. on aminocarb - effects on environmental quality. Edited by V.N. Mallet. University of Moncton, N.B. pp. 12-30. (cf. Bull. Environm. Contam. Toxicol. 24: 415-422).

Marancik, J. 1976. Effects of insecticides used for spruce budworm control in 1975 on fish. In Cooperative pilot control project of Dylox, Matacil and Sumithion for spruce budworm control in Maine, 1975. Forest Insect and Disease Management, U.S. Forest Service. pp. 11-34.

Mathieu, P. and Provencher, M. 1978. Etude des impacts des pulvérisations aériennes d'insecticide sur les écosystèmes aquatics - le lac Ste-Anne - Printemps 1977. Ministère des Richesses Naturelles, P.Q.

McLeese, D.W. 1980. Uptake and excretion of aminocarb, nonyl phenol and pesticide diluent 585 by mussels (Mytilus edulis). In Environmental surveillance in New Brunswick 1978-79: effects of spray operations for forest protection against spruce budworm. Edited by I.W. Varty. University of New Brunswick, N.B. p. 60.

McLeese, D.W., Zitko, V. and Peterson, M.R. 1979. Structure-lethality for phenols, anilines and other aromatic compounds in shrimp and clams. Chemosphere 8: 53-57.

McLeese, D.W., Zitko, V., Metcalf, C.D. and Sergeant, D.B. 1980a. Lethality of aminocarb and the components of the aminocarb formulation to juvenile Atlantic salmon, marine invertebrates and freshwater clams. Chemosphere 9: 79-82.

McLeese, D.W., Sergeant, D.B., Metcalfe, C.D., Zitko, V. and Burridge, L.E. 1980b. Uptake and excretion of aminocarb, nonyl phenol, and pesticide diluent oil 585 by mussels (Mytilus edulis). Bull. Environ. Contam. Toxicol. 24: 575-581.

McLeese, D.W., Zitko, V., Sergeant, D.B., Burridge, L. and Metcalfe, C.D. 1981. Lethality and accumulation of alkylphenols in aquatic fauna. Chemosphere 10: 723-730.

McLeod, B.B. 1978. Effects of aminocarb on honey bees. In Environmental surveillance of insecticide spray operations in New Brunswick's budworm-infested forests, 1977. Edited by I.W. Varty. Canada Forestry Service Rep. M-X-87. p. 11.

McLeod, B.B. and Mortensen, K.L. 1975. Honey bees. In Studies of the environmental impact of the 1974 spruce budworm control operation in Quebec. Edited by C.H. Buckner and R. Sarrazin. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-93: 76-79.

McMahon, T.A., Brain, J.D. and Lemott, S. 1977. Species differences in aerosol deposition. In Inhaled Particles IV. Part 1. Edited by W.H. Walton. British Occupational Hygiene Society, Surrey, England.

McNeil, J.N. and McLeod, J.M. 1977. Apparent impact of fenitrothion on the Swaine jack-pine sawfly, Neodiprion swainei. In Proc. Symp. on Fenitrothion: the long term effects of its use in forest ecosystems. NRCC No. 16073. pp. 203-216.

Meeh, K. 1897. Oberflaechenmessugen des menschlichen Koerpers. Z. Biol. 15: 425-458.

Miller, C.A. 1963. Parasites and the spruce budworm. In The dynamics of epidemic spruce budworm populations. Edited by R.F. Morris. Mem. Entomol. Soc. Can. 31: 228-243.

Millikin, R.L. 1981. Preliminary report on the impact of Matacil formulations on terrestrial invertebrates, Bathurst, New Brunswick. Forest Pest Management Institute. File Report No. 15.

Minor, R.G. 1978. Metabolism of Matacil in soil and in aquatic environment. Mobay Chem. Corp. Report 50427.

Misener, R.L. 1981. Personal communication to R. Gosselin. Chemagro Ltd., Mississauga, Ont.

Miyamoto, J., Sato, Y., Yamamato, K. and Suzuki, S. 1968. Activation and degradation of Sumithion, methyl parathion and their oxygen analogues by mammalian enzymes in vitro. Botyu-Kagaku 33: 1-7.

Mobay Chemical Corporation (undated). Phytoplankton productivity, oyster shell growth. Mobay Chem. Corp. Report 11106.

Mobay Chemical Corporation. 1961. Compound Bayer 44646. Mobay Chem. Corp. Report 7902.

Mobay Chemical Corporation. 1966. Matacil active ingredient. Mobay Chem. Corp. Report 18189.

Mobay Chemical Corporation. 1979. Technical information sheet.

Mobay Chemical Corporation. 1981. Interim Report.

Montreal Engineering Co. Ltd. 1976. Assessment of selected insecticide application on the drift of stream macroinvertebrates. Report to the New Brunswick Dept. of Natural Resources, Fredericton, N.B. 18 pp.

Montreal Engineering Co. Ltd. 1978. Assessment of the effects of the 1977 New Brunswick spruce budworm control program on fish pond organisms and fish growth. Report to the New Brunswick Dept. of Natural Resources, Fredericton, N.B. 39 pp.

Morris, R.F. 1963. The dynamics of epidemic spruce budworm populations. Mem. Entomol. Soc. Can. 31. 332 pp.

Mulkey, N.S., McPhaul, L., Augenstein, L.L. and Wargo, J.P. 1978. Photodegradation of ^{14}C-Matacil in aqueous solution. Mobay Chem. Corp. Report 50447.

Mullen, P.W. 1978. Immunopharmacological considerations in Reye's syndrome: a possible xenobiotics initiated disorder. Biochem. Pharmacol. 27: 145-9.

Murphy, J.J., Minor, R.G., Jacobs, K. and Shaw, H.R. 1975a. Persistence of Matacil in soil. Mobay Chem. Corp. 43444.

Murphy, J.J., Jacobs, K. and Minor, R.G. 1975b. Stability of Matacil in aqueous systems. Mobay Chem. Corp. Report 43450.

Nagel, C.D., Tessier, J.F., McPhaul, L., Augenstein, L.L. and Wargo, J.P. 1978. Spruce foliage study with ^{14}C-Matacil. Mobay Chem. Corp. Report 50445.

Natoff, I.L. and Reiff, B. 1973. Effect of oximes on the acute toxicity of anticholinesterase carbamates. Toxicol. Appl. Pharmacol. 25: 569-575.

Needham, P.R. and Usinger, R.L. 1956. Variability of the macro fauna of a single ripple in Prosser Creek, California, as indicated by the Surber sampler. Hilgardia 24: 383-409.

Neely, W.B. 1979. A preliminary assessment of the environmental exposure to be expected from the addition of a chemical to a simulated aquatic ecosystem. Int. J. Environ. Stud. 13: 101-108.

Neely, W.B., Branson, D.R. and Blau, G.E. 1974. Partition coefficients to measure bioconcentration potential of organic chemicals in fish. Environ. Sci. Technol. 8: 1113-1115.

Nelson, D.L. 1965. Systemic effect of Bay 44646 applied to the conjunctival sac of dogs. Mobay Chem. Corp. Report 15233.

Nelson, D.L. 1978a. Acute toxicity of Matacil 1.8-585 to Daphnia magna. Mobay Chem. Corp. Report 66230.

Nelson, D.L. 1978b. Acute toxicity of Matacil technical to Daphnia magna. Mobay Chem. Corp. Report 66103.

Nelson, D.L. 1978c. Acute rate cholinesterase no-effect study with Matacil technical. Mobay Chem. Corp. Report 66517.

Nelson, D.L. 1978d. Acute oral toxicity of Matacil technical and Matacil analytical grade to female rats. Mobay Chem. Corp. Report 66102.

Nelson, D.L. 1978e. Acute oral toxicity of Matacil 1.8-585 to rats. Mobay Chem. Corp. Report 66106.

Nelson, D.L. 1978f. Acute oral toxicity of Matacil 1.8D (Canada) room temperature sample and freezer sample to rats. Mobay Chem. Corp. Report 66108.

Nelson, D.L. 1978g. Acute dermal toxicity of Matacil 1.8-585 to rabbits. Mobay Chem. Corp. Report 66107.

Nelson, D.L. 1978h. Acute inhalation toxicity of Matacil 1.8-585 to rats. Mobay Chem. Corp. Report 66105.

Nelson, D.L. 1978i. Eye and dermal irritancy of Matacil 1.8-585. Mobay Chem. Corp. Report 66104.

Nelson, D.L. and Burke, M.A. 1977a. Acute dermal toxicity of Matacil 1.4 OSC. Mobay Chem. Corp. Report 54082.

Nelson, D.L. and Burke, M.A. 1977b. Eye and dermal irritancy of Matacil 1.4 OSC. Mobay Chem. Corp. Report 54081.

Nelson, D.L. and Matzkanin, C.S. 1977. The acute oral toxicity of Matacil 1.4 OSC. Mobay Chem. Corp. Report 53957.

Nelson, D.L. and Roney, D.J. 1978a. Acute toxicity of Matacil 1.8-585 (Canada) to bluegill and rainbow trout. Mobay Chem. Corp. Report 66044.

Nelson, D.L. and Roney, D.J. 1978b. Acute toxicity of Matacil technical Matacil 1.4 oil soluble concentrate, Matacil 1.8 oil soluble concentrate, and the inert ingredients of Matacil 1.4 and 1.8 oil soluble concentrates to rainbow trout. Mobay Chem. Corp. Report 66045.

Nelson, D.L. and Roney, D.J. 1978c. Acute toxicity of Matacil Technical, Matacil 1.4 OSC, Matacil 1.8 OSC, and the inert ingredients of Matacil 1.4 and 1.8 OSC to channel catfish. Mobay Chem. Corp. Report 65829.

Nelson, D.L. and Roney, D.J. 1979. Acute toxicity of end use dilution of Matacil 1.5-585 (Canada) to bluegill and rainbow trout. Mobay Chem. Corp. Report 67997.

Nelson, D.B., Sullivan-Bolai, J.Z., Marks, J.S., Morens, D.M. and Schonberger, L. 1979. Reye's syndrome: an epidemiologic assessment based on national surveillance 1977-1978 and a population based study in Ohio, 1973-1977. In Reye's syndrome II. Edited by J.F.S Crocker. Grune and Stratton, New York. pp. 33-51.

Newlands, M.J., Mackey, M.D. and Cook, A. 1979. Unpublished data supplied to Panel.

Nice, M.M. 1938. The biological significance of bird weights. Bird Banding 9: 1-11.

Nigam, P.C. 1975. Strategic chemicals for protection of coniferous forests from insect pests. Chem. Control Res. Inst., Ottawa. Inf. Report CC-X-60.

Nigam, P.C. 1980. Use of chemical insecticides against the spruce budworm in eastern Canada. CANUSA Newsletter. 11: 1-3.

Noel, P.R.B., Mawdesley-Thomas, L.E., Chesterman, H., Clarke, D. and Street, A.E. 1966. BAY 44646 - chronic oral toxicity study in dogs. Mobay Chem. Corp. Report 18996.

NRCC. 1975. Fenitrothion: the effects of its use on environmental quality and its chemistry. Associate Committee on Scientific Criteria for Environmental Quality. National Research Council of Canada. NRCC No. 14104. 162 pp.

NRCC. 1979. Carbofuran: criteria for interpreting the effects of its use on environmental quality. Associate Committee on Scientific Criteria for Environmental Quality. National Research Council of Canada. NRCC. No. 16740. 191 pp.

NRCC. 1981. Pesticide-pollinator interactions. Associate Committee on Scientific Criteria for Environmental Quality. National Research Council of Canada. NRCC No. 18471. 190 pp.

O'Brien, R.D. 1960. Toxic phosphorus esters. Academic Press, London.

O'Brien, R.D. 1967. Insecticides action and metabolism. Academic Press, London.

O'Brien, R.D. 1968. Kinetics of the carbamylation of cholinesterase. Mol. Pharmacol. 4: 121.

OECD. 1982. OECD Expert Committee on Neurotoxicology. Washington, April 22-25.

Olson, T.J. 1964. A colorimetric method for the determination of Bayer 44646 residues in soil. Mobay Chem. Corp. Report 13454.

Oonnithan, E.S. and Casida, J.E. 1966. Metabolites of methyl-and dimethyl-carbamate insecticide chemicals as formed by rat liver microsomes. Bull. Environ. Contam. Toxicol. 1: 59-69.

Oonnithan, E.S. and Casida, J.E. 1968. Oxidation of methyl- and dimethyl-carbamate insecticide chemicals by microsomal enzymes and anticholinesterase activity of the metabolites. J. Agric. Food Chem. 16: 28-44.

Osborne, J. 1979. Aquatic systems. In Environmental monitoring spruce budworm spray program in Newfoundland - 1978. Nfld. Dept. of Consumer Affairs and Environment. Inf. Report RA-79-2. pp. 25-27.

Osborne, J. 1981. Information supplied to Panel. Environmental Protection Service, St. John's, Nfld.

Otvos, I.S. and Raske, A.G. 1980. The effects of fenitrothion, Matacil and Bacillus thuringiensis plus Orthene on larval parasites of the spruce budworm, Choristoneura fumiferana. Can. For. Serv. Inf. Report N-X-184.

Palmer, A.K. and Fletcher, M.A. 1966. Effect of Bayer 44646 upon reproduction of multiple rat generations. Mobay Chem. Corp. Report 19216.

Parker, B., Hindley, B., Fenton, M.J., Young, R., Kohli, M. and Tanner, J. 1980. Environmental monitoring of the Ontario Ministry of Natural Resources spruce budworm spraying program, Kirkland 1980. Ontario Ministry of Natural Resources.

Partin, J.C. 1975. Reye's syndrome (encephalopathy and fatty liver). Gastroenterology 69: 511-518.

Patel, N. 1978. The composition of technical Matacil. Mobay Chem. Corp. Report 67418.

Pearce, P.A. 1968. Effects on bird populations of phosphamidon and Sumithion used for spruce budworm control in New Brunswick and hemlock looper control in Newfoundland in 1968: a summary statement. Can. Wildl. Serv. Rep. Ser. 14.

Pearce, P.A. 1970. Summary of Canadian Wildlife Service supported projects - 1970. New Brunswick spruce budworm control program. Interdepartmental Committee on Forest Spraying Operations.

Pearce, P.A. 1971. Effects of Matacil and fenitrothion spraying on birds in New Brunswick and Quebec 1971. Interdepartmental Committee on Forest Spraying Operations.

Pearce, P.A. and Brun, G.L. 1980. Off target fallout of aminocarb in rain. In Environmental surveillance in New Brunswick, 1978-1979: effects of spray operations for forest protection. Edited by I.W. Varty. University of New Brunswick, N.B. pp. 69-70.

Pearce, P.A. and Garrity, N.R. 1981. Impact of aminocarb (Matacil) spraying on forest birds in Northern New Brunswick. Can. Wildl. Serv. Prog. Notes. (In press)

Pearce, P.A., Peakall, D.B. and Erskine, A.J. 1976. Impact on forest birds of the 1975 spruce budworm spray program in New Brunswick. Can. Wildl. Serv. Notes No. 62.

Pearce, P.A., Peakall, D.B. and Erskine, A.J. 1979. Impact on forest birds of the 1976 spruce budworm spray operation in New Brunswick. Can. Wildl. Serv. Prog. Notes No. 97.

Pearce, P.A., Brun, G.L. and Witteman, J. 1980. Off target fallout of fenitrothion in rain. In Environmental surveillance in New Brunswick, 1978-1979: effects of spray operations for forest protection. Edited by I.W. Varty. University of New Brunswick, N.B.

Penny, G.H. 1971a. Report on the effects of the 1970 New Brunswick forest spraying on juvenile salmon and their food organisms. Dep. Fish. For. Can. Rep. 71-13. 41 pp.

Penny, G.H. 1971b. Effects of aerial forest spraying in New Brunswick in 1971 with the carbamate insecticide Matacil on aquatic stream invertebrates. Dept. Environ. Report 71-19. 13 pp.

Peters, J.P. and Van Slyke, D.D. 1946. Quantitative clinical chemistry. Interpretation. Volume 1, 2nd edition. Williams and Wilkins Co., Baltimore.

Peterson, J.W. 1976. The effect of Dylox, Matacil, Sumithion on birds, small mammals and amphibians. In Cooperative pilot control project of Dylox, Matacil and Sumithion for spruce budworm control in Maine, 1975. Forest Insect and Disease Management, U.S. Forest Service. pp. 2-10.

Picot, J.C.C. and Kristmanson, D.D. 1980. Aerial spraying of coniferous forests - a model for disperson and deposition. University of New Brunswick. Dept. of Chemical Engineering Report.

Picot, J.J.C., Kristmanson, D.D., Chitrangad, B. and Henderson, G. 1980. Near field drift in aerial spraying. University of New Brunswick. Dept. of Chemical Engineering Report, February 1980.

Picot, J.C.C., Chitrangad, B. and Henderson, G. 1981. Evaporation rate correlation for atomized droplets. Trans. ASAE 24: 552-554.

Plowright, R.C. 1980. Annual and seasonal trends in bumble bee abundance and flowering plant reproduction associated with aerial spray operations in New Brunswick. In Environmental surveillance in New Brunswick, 1978-79: effects of spray operations for forest protection against spruce budworm. Edited by I.W. Varty. University of New Brunswick, N.B. pp. 37-40.

Plowright, R.C. and Pendrel, B.A. 1978. A comparison of the effects of aminocarb and fenitrothion on forest pollinators in New Brunswick. In Proc. Symp. Aminocarb - Effects of its use on environmental quality. Edited by V.N. Mallet. University of New Brunswick, N.B. pp. 118-124.

Plowright, R.C. and Rodd, F.H. 1980. The effect of aerial insecticide spraying on hymenopterous pollinators in New Brunswick. Can. Entomol. 112: 259-269.

Plowright, R.C., Pendrel, B.A. and McLaren, I.A. 1978. The impact of aerial fenitrothion spraying upon the population biology of bumble bees in southwestern New Brunswick. Can. Entomol. 110: 1145-1156.

Pollack, J.D. 1979. Models of chemical and virus interaction and their relation to a multiple etiology of Reye's syndrome. In Reye's syndrome II. Edited by J.F.S. Crocker. Grune and Stratton, New York. pp. 341-360.

Prasad, R. (undated). Effects of nonyl phenol on aquatic plants. Forest Pest Management Institute.

Prasad, R. 1981. Information supplied to Panel. Forest Pest Management Institute, Sault St. Marie, Ont.

Prebble, M.L. 1975. Aerial control of forest insects in Canada. Dept. of the Environment, Ottawa.

Qadri, S.U. and Richardson, G.M. 1980. The dynamics and effects of Matacil in benthic invertebrates and benthophagous fish. In Fate of Matacil in aquatic ecosystems. Biology Dept., University of Ottawa.

Quarles, J.M. and Tennant, R.W. 1975. Effects of nitrosocarbaryl on BALB/373 cells. Cancer Res. 35: 2637-2645.

Rabeni, C.F. and Gibbs, K.E. 1976. Effects of Dylox, Matacil and Sumithion on non-target stream insects in Maine, 1975. In Cooperative pilot control project of Dylox, Matacil and Sumithion for spruce budworm control in Maine. Forest Insect and Disease Management, U.S. Forest Service. pp. 64-74.

Randall, A.P. 1973. Studies on the control of the spruce budworm by aerial application of chemicals. Report of Annual Forest Pest Control Forum, Ottawa. Appendix 18.

Regan, J.D., Settoa, R.B., Francis, A.A. and Lijinsky, W. 1976. Nitrosocarbaryl: its effect on human DNA. Mutat. Res. 38: 293-302.

Reid, J.D. and Crabbe, R.S. 1980. Two methods of long range drift of forest pesticide aerial spray. Atmos. Environ. 14: 1017-1025.

Reuben, F.L. 1979. Recent developments and contributions from experimental models of Reye's syndrome. In Reye's syndrome II. Edited by J.F.S. Crocker. Grune and Stratton, New York. pp. 385-397.

Reye, R.D.K., Morgan, G. and Baral, J. 1963. Encephalopathy and fatty degeneration of the viscera, a disease entity in childhood. Lancet 2: 749-752.

Rick, A.M. and Price, I.M. 1974. Amphibian and reptile monitoring during the 1969-1971 New Brunswick spruce budworm spray program. In Pesticide Section. Can. Wildl. Serv. Manuscript Rep. Ser. 30. 9 pp.

Rickard, R.W. 1979. Chemical properties and potential toxicological significance of N-nitrosocarbamates. Ph.D. dissertation, University of Kentucky, Lexington, Kentucky.

Rittenhouse, J.W., Mason, M. and Baublis, J.V. 1979. Amino acid ratios in Reye's syndrome. Lancet 2: 105-106.

Roan, C.C., Morgan, P.P., Cook, N. and Paschal, E.H. 1969. Blood cholinesterase, serum parathion concentrations and urine p-nitrophenol concentrations in exposed individuals. Bull. Environ. Contam. Toxicol. 4: 362-369.

Roberts, J.R., Mitchell, M.F., Boddington, M.J. and Ridgeway, J.M. 1981. A screen for the relative persistence of lipophilic organic chemicals in aquatic ecosystems - Part 1. In A simple computer model as a screen for persistence. Associate Committee on Scientific Criteria for Environmental Quality. National Research Council of Canada. NRCC No. 18570.

Robinson, D. 1968. Three-generation reproductive study in the hen. Mobay Chem. Corp. Report 68384.

Robinson, K., Breckenbridge, C. and Procter, B.G. 1980. A study of the teratogenic potential of Matacil in the gravid rat. Mobay Chem. Corp. Report 69203.

Rohm and Haas Company. 1975. Data sheet for alkylphenols.

Root, M., Cowan, J. and Doull, J. 1963. Subacute oral toxicity of Bayer 44646 to male and female rats. Mobay Chem. Corp. Report 11161.

Rozee, K.R., Lee, S.H.S., Crocker, J.F.S. and Safe, S.M. 1978. Enhanced virus replication in mammalian cells exposed to commercial emulsifiers. Appl. Environ. Microbiol. 35: 297-300.

Rozee, K.R., Laltoo, M., Lee, S.H.S., Crocker, J.F.S. and Safe, S.H. 1979. Emulsifiers as enhancement factors in virus virulence. In Reye's syndrome II. Edited by J.F.S. Crocker. Grune and Stratton, New York. pp. 434-457.

Rozee, K.R., Lee, S.H.S., Arcinue, E. and Crocker, J.F.S. 1981. A compromised interferon response: an etiologic factor in Reye's syndrome. Pediatr. Res. 15: 609.

Rozee, K.R., Lee, S.H.S., Crocker, J.F.S., Digout, S. and Arcinue, E. 1982. Is a compromised interferon response an etiologic factor in Reye's syndrome? Can. Med. Assoc. J. 126: 798-802.

Rubner, M. 1902. The laws of energy consumption in nutrition. Franz Deuticke, Leipzig und Vienna. Edited by R.J.T. Joy, U.S. Army Res. Inst. Environ. Med., Natick, Mass. 1968.

Ryan, N.J., Hogan, G.R., Haynes, A.W., Unger, P.D. and Siraj, M.Y. 1979. Aflatoxin B_1: Its role in the etiology of Reye's syndrome. Pediatrics 64: 71-75.

Sanders, H.O. 1969. Toxicity of pesticides to the crustacean Gammarus lacustrus. USDI Tech. paper of the Bureau of Sport Fisheries and Wildlife.

Sarrazin, R. 1977. Effets environnementaux, des pulverisation airiennes contre la tordeuse des bourgions de l'épinette au Québec - 1977. Ministère du Tourisme, de la Chasse et de la Pêche Direction de la Général de la Faune, Québec. Rapport de Recherche Faunique No. 15.

Sarrazin, R. 1978. Effets environnementaux des pulvérisations aériennes contre la tordeuse des bourgeons de l'épinette au Québec - 1978. Ministère du Tourisme, de la Chasse et de la Pêche, Direction de la Général de la Faune, Québec. Rapport de Recherche Faunique No. 36. 27 pp.

Schafer, E.W. 1972. The acute oral toxicity of 369 pesticidal, pharmaceutical and other chemicals to wild birds. Toxicol. Appl. Pharmacol. 21: 315-330.

Schafer, E.W. and Cunningham, D.J. 1972. An evaluation of 148 compounds as avian immobilizing agents. U.S. Dept. of the Interior Fish and Wildlife Service. Special Scientific Report. Wildlife No. 150. Washington, D.C.

Schoettger, R.A. and Mauck, W.L. 1978. Toxicity of experimental forest insecticides to fish and aquatic invertebrates. In Proc 1st and 2nd USA-USSR symposia on effects of pollutants upon aquatic ecosystems. EPA-600/3-78-076. pp. 11-27.

Seiler, J.P. 1977. Nitrosation in vitro and in vivo by sodium nitrite and mutagenicity of nitrogenous pesticides. Mutat. Res. 48: 225-236.

Shaw, H.R. 1978. Metabolism of Matacil in swine. Mobay Chem. Corp. Report 50426.

Shaywitz, B.A., Venes, J., Cohen, D.J. and Bowers, M.B. 1979. Reye syndrome: monoamine metabolites in ventricular fluid. Neurology (Minneap) 29: 467-72.

Shell Chemical of Canada. (undated). Data sheet on various petroleum products.

Shell Chemical of Canada. 1981. Information supplied to panel.

Smith, J.H., Bomberger, D.C. and Haynes, D.L. 1980. Prediction of the volatililzation rates of high-volatility chemicals from natural water bodies. Environ. Sci. Technol. 14: 1332-1337.

Smith, J.L., Elvare, E. and Frazier, W.H. 1930a. The pharmacological action of certain phenol esters, with special reference to the etiology of so called Ginger Paralysis. Public Health Rep. 45: 2509-2524.

Smith, M.I., Elvare, E., Valaer, P.J., Frazier, W.M. and Mallory, G.E. 1930b. Pharmacological and chemical studies of the cause of so called Ginger Paralysis. Public Health Rep. 45: 1703-1723.

Smyth, H.Jr., Carpenter, C., Weil, C., Pozzani, U., and Striegel, J. 1962. Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23(2): 96.

Smyth, H. Jr., Carpenter, C., Weil, C., Pozzani, U., Striegel, J. and Nycum, J. 1969. Range-finding toxicity data: List VII. Am. Ind. Hyg. Assoc. J. 30(5): 471.

Snyder, W.S., Cook, M.J., Nasset, E.S., Karhavsen, L.R., Howells, G.P. and Tipton, I.H. 1974. Report of the task group on reference man. ICRP publication 23. Pergamon Press, Oxford. 480 pp.

Southwood, T.R.E. 1966. Ecological methods. Methuen and Co., London.

Stanley, C.W. and Delphia, L.M. 1978. Gas liquid chromatographic method for detecting residues of Matacil in spruce needles, fish, soil and water. Mobay Chem. Corp. Report 66512.

Stanley, C.W. and Delphia, L.M. 1981. Matacil residue determination in foliage, fish, soil and water. J. Agric. Food Chem. 29: 1038-1039.

Stewart, P.A. 1937. A preliminary list of bird weights. Auk 54: 324-332.

Strankowski, K.J. and Minor, R.G. 1978. Effect of Matacil on isolated soil microorganisms. Mobay Chem. Corp. Report 66244.

Strother, A. 1970. Comparative metabolism of selected N-methylcarbamates by human and rat liver fractions. Biochem. Pharmacol. 19: 2525-2529.

Strother, A. 1972. In vitro metabolism of methylcarbamate insecticides by human and rat liver fraction. Toxicol. Appl. Pharamcol. 21: 112-129.

Sundaram, K.M.S. 1976. Chemical analysis of Matacil in fish samples received from the accident investigation team of Quebec government. Canada Forestry Service File Report No. 54. 13 pp.

Sundaram, K.M.S. 1981. Distribution, persistence and fate of Matacil formulations in a forest ecosystem. Forest Pest Management Institute. Report No. 20. 27 pp.

Sundaram, K.M.S. and Hopewell, W.W. 1977. Fate and persistence of aminocarb in conifer foliage and forest soil after simulated aerial spray application. Forest Pest Management Institute. Dept. of Environment Report FPM-X-6.

Sundaram, K.M.S. and Szeto, S.Y. 1979. A study of the lethal toxicity of aminocarb to freshwater crayfish and its in vitro metabolism. J. Environ. Sci. Health B14: 589-602.

Sundaram, K.M.S., Volpe, Y., Smith, G.C. and Duffy, J.R. 1976. A preliminary study on the persistence and distribution of Matacil in a forest environment. Canadian Forestry Service. Environ. Canada Report CC-X-116.

Sundaram, K.M.S., Szeto, S. and Hindle, R. 1978. Isolation and analysis of aminocarb and its phenol from environmental waters. Forest Pest Management Institute. Report FPM-X-18.

Sundaram, K.M.S., Szeto, S.Y. and Hindle, R. 1979. Evaluation of XAD-2 as the extractant for carbamate insecticides from natural waters. J. Chromatogr. 177: 23-24.

Sundaram, K.M.S., Szeto, S., Hindle, R. and McTavish, D. 1980. Residues of nonyl phenol in spruce foliage, forest soil, stream water and sediment after its aerial application. J. Environ. Sci. Health B15: 403-419.

Surber, E.W. 1936. Rainbow trout and bottom fauna production in one mile of stream. Trans. Am. Fish. Soc. 66: 193-202.

Symons, P.E.K. 1977. Dispersal and toxicology of the insecticide fenitrothion predicting hazards of forest spraying. Residue Rev. 68: 1-36.

Szeto, S.Y. and Holmes, S.B. 1982. The lethal toxicity of Matacil 1.8F to rainbow trout. J. Environ. Sci. Health B17: 51-61.

Szeto, S.Y. and Sundaram, K.M.S. 1980. Simplified method for the analysis of some carbamate insecticides in foliage, forest soil and fish tissue by direct gas-liquid chromatography. J. Chromatogr. 200: 179-184.

Task Group on Lung Dynamics. 1966. Deposition and retention models for internal dosimetry of the human respiratory tract. A report prepared for the International Commission on Radiological Protection. Health Phys. 12: 173-207.

Tate, R.L. and Alexander, M. 1976. Formation of dimethylamine and diethylamine in soil treated with pesticides. Soil Sci. 118: 317-321.

Tennankore, K., Picot, J.J.C., Chitrangad, B. and Kristmanson, D.D. 1980. Aircraft vortex studies in forest aerial spraying. Trans. ASAE 23: 1076-1083.

Tessier, J.F., Mulkey, W.S., Augenstein, L.L. and Waryo, J.P. 1978. ^{14}C-Matacil buffer hydrolysis study. Mobay Chem. Corp. Report 50444.

Thaler, G.R. and Plowright, R.C. 1980. The effect of aerial insecticide spraying for spruce budworm control on the fecundity of entomophilous plants in New Brunswick. Can. J. Bot. 58: 2022-2027.

Thaler, M.M., Bruhn, F.W., Applebaum, M.N. and Goodman, J. 1970. Reye's syndrome in twins. J. Pediatr. 77: 638-646.

Thaler, M.M., Hoogenraad, H.J. and Boswell, M. 1974. Reye's syndrome due to a navel protein tolerant variant of armithine transcarbamylase deficiency. Lancet 2: 438-440.

Thomas, R. and Kimmerle, G. 1974. Metabolites of the insecticide Matacil and their acute toxicity. Mobay Chem. Corp. Report 43065.

Thorpe, E.J. 1980. Effects of spraying of solitary bee populations in forests. In Environmental surveillance in New Brunswick 1978-79: effects of spray operations for forest protection. Edited by I.W. Varty. Univ. of New Brunswick, N.B. pp. 41-42.

Thorpe, E. and Varty, I.W. 1978. Solitary bees. In Environmental surveillance of insecticide spray operations in New Brunswick's budworm infested forest, 1977. Edited by I.W. Varty. Canada Forestry Service Report M-X-87 pp. 11-13.

Tomney, T.D., Smedley, J.B., Kristmanson, D.D. and Picot, J.J.C. 1978. The characteristics of drop-size distributions generated by aerial spray atomizers. University of New Brunswick. Dept. of Chemical Engineering Report, July 1978.

Tower, D.B. 1979. Discussion on animal model for Reye's syndrome. In Reye's syndrome II. Edited by J.F.S. Crocker. Grune and Stratton, New York. pp. 393-394.

Trauner, D.A., Stockard, J.J. and Sweetman, L. 1977. EEG correlation with biochemical abnormalities in Reye's syndrome. Arch. Neurol. 34: 321.

Tsukamoto, M. and Casida, J.E. 1967. Metabolism of methylcarbamate insecticides by the $NADPH_2$ - requiring enzyme system from houseflies. Nature 213: 49-51.

Tucker, R.K. and Crabtree, D.G. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Dept. Interior. Fish. Wildlife Resource Pub. 84.

Udenfriend, S., Clark, C.T., Axelord, J. and Brodie, B.B. 1954. Ascorbic acid in aromatic hydroxylation. 1. A model system in aromatic hydoxylation. J. Biol. Chem. 208: 731-739.

Varty, I.W. 1976. Environmental effects of spruce budworm spray program in New Brunswick, 1976. Canada Forestry Service Report M-X-67.

Varty, I.W. 1977. Long-term effects of fenitrothion spray programs on non-target terrestrial arthropods. In Proceedings of a Symposium on Fenitrothion: The long-term effects of its use in forest ecosystems. Edited by J.R Roberts, R. Greenhalgh and W.K. Marshall. National Research Council of Canada. NRCC No. 16073. pp. 343-375.

Varty, I.W. 1978. Hazard to non-target insects. In Environmental effects of the spruce budworm spray program in New Brunswick, 1976. Edited by I.W. Varty. Canada Forestry Service Report M-X-67. pp. 14-15.

Varty, I.W. 1980. Environmental surveillance in New Brunswick 1978-1979. Effects of spray operations for forest protection. Univ. of New Brunswick, N.B.

Varty, I.W. 1981. Data submitted to Panel. University of New Brunswick.

Varty, I.W. 1982. Information submitted to Panel. University of New Brunswick.

Webb, F.E. 1980. Information supplied to Panel. Forest Protection Ltd., N.B.

Weinberger, P. and Greenhalgh, R. 1981. Unpublished data submitted to Panel. University of Ottawa, Ont.

Weinberger, P. and Ouelette, H. 1981. Persistence degradation and accumulation of Matacil in two compartment water/plant microcosms. Part II. In The fate of Matacil in aquatic ecosystems. University of Ottawa, Ottawa, Ont.

Weinberger, P. and Rea, M. 1981. Nonylphenol: A perturbant additive to an aquatic ecosystem. In Proc. 7th Annual Aquatic Toxicity Workshop, Montreal, Québec. Canadian Technical Report of Fisheries and Aquatic Sciences No. 990. pp. 369-381.

Weinberger, P., Englehardt, R., Philogène, B. and Qadri, S. 1980. The fate of Matacil in aquatic ecosystems. University of Ottawa, Ont.

Wells, P.G., Matheson, R.A., Lord, D.A. and Doe, K.G. 1979. Environmental monitoring of the 1978 spruce budworm spray program in New Brunswick, Canada - field sampling and aquatic toxicity studies with fish. Environmental Protection Service. EPS-5-AR-79-1.

Wesley, M.L., Hicks, B.B., Dannevik, W.P., Frisella, S. and Husar, R.B. 1977. An eddy-correlation measurement of particulate deposition from the atmosphere. Atmos. Environ. 11: 561-563.

Wheeler, L. and Strother, A. 1969. Chromatography of N-methyl carbamates in the gasious phase. J. Chromatogr. 45: 362-370.

Whitman, W.R. 1978. Effects of aminocarb in ponds. In Environmental surveillance of insecticide spray operations in New Brunswick budworm infested forests. 1977. Edited by I.W. Varty. Maritimes Forest Research Centre. Inf. Report M-X-87. p. 9.

Wickens, R. 1980. A streamtube concept for lift: With reference to the maximum size and configuration of aerial spray emissions. Can. Aeronaut. Space J. 26(2): 135-143.

Wildish, D.J. 1980. Matacil and long-term microbiological side-effects in freshwater ponds. In Environmental surveillance in New Brunswick: effects of spray operations for forest protection. Edited by I.W. Varty. University of New Brunswick. N.B. p. 53.

Wildish, D.J. and Elner, J.K. 1981. Absence of long-term changes in the microbiology of freshwater ponds treated with Matacil. Can. Tech. Rep. Fish. Aquat. Sci. No. 1049. 17 pp.

Williams, E., Markle, R.W. and Redemann, C.T. 1964. Identification of metabolites of Zectran insecticides in dog urine. J. Agric. Food Chem. 12: 457-461.

Wilson, I.B., Hatch, M.A. and Ginsburg, S. 1960. Carbamylation of acetylcholinesterase. J. Biol. Chem. 235: 2321.

Woodward, D.F. and Mauck, W.L. 1980. Toxicity of five forest insecticides to cutthroat trout and two species of aquatic invertebrates. Bull. Environ. Contam. Toxicol. 25: 846-853.

Zepp, R.G. and Cline, D.M. 1977. Rates of direct photolysis in aquatic environments. Curr. Res. 11: 359-366.

Zitko, V., McLeese, D.W. and Sergeant, D.B. 1980. Lethality of aminocarb and its formulation to juvenile Atlantic salmon and marine invertebrates. In Environmental surveillance in New Brunswick 1978-79: effects of spray operations for forest protection. Edited by I.W. Varty. University of New Brunswick, N.B.

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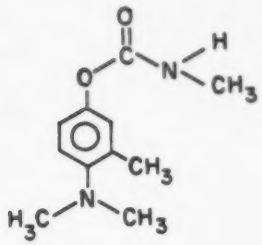

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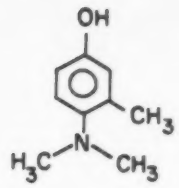

C

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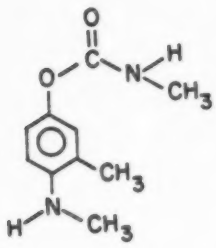

MAA

3-methyl-4-(methylamino)phenyl-N-methylcarbamate
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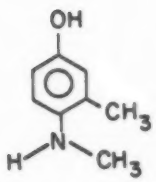
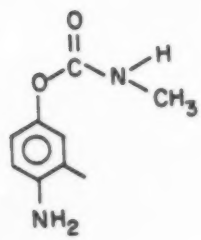


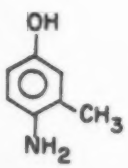
MAC

3-methyl-4-(methylamino)phenol
[not listed]



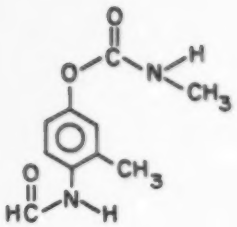
AA

4-amino-3-methylphenyl-N-methylcarbamate
[10233-97-3]



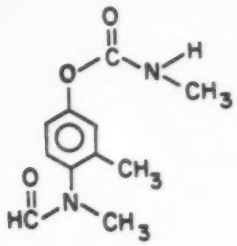
AC

4-amino-3-methylphenol
[2835-99-6]



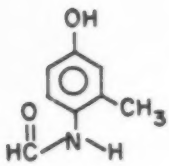
FA

4-formamido-3-methylphenyl-N-methylcarbamate
[10234-35-2]



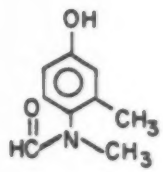
MFA

4-methylformamido-3-methylphenyl-N-methylcarbamate
[10233-98-4]



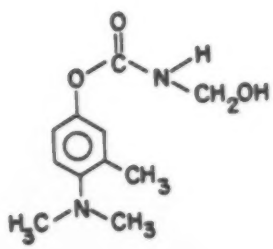
FC

N-(4-hydroxy-2-methylphenyl)formamide
[60463-08-3]



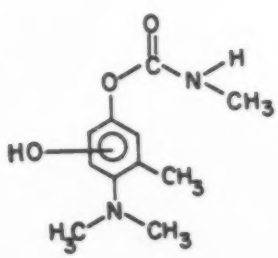
MFC

N-(4-hydroxy-2-methylphenyl)-N-methylformamide
[not listed]



HNA

4-(dimethylamino)-3-methylphenyl-N-hydroxymethylcarbamate
[19809-46-2]



HA

benzenediol, (dimethylamino)methyl-mono(methylcarbamate) (ester)

[52174-60-4]